COMPARISON OF POST CESAREAN ANALGESIA WITH EPIDURAL BUPIVACAINE-FENTANYL V/S BUPIVACAINE-NALBUPHINE V/S BUPIVACAINE-BUTORPHANOL – A DOUBLE BLINDED RANDOMIZED STUDY

Dissertation submitted

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CERTIFICATE

This is to certify that this dissertation titled **"COMPARISON OF POST CESAREAN ANALGESIA WITH EPIDURAL BUPIVACAINE-FENTANYL V/S BUPIVACAINE-NALBUPHINE V/S BUPIVACAINE - BUTORPHANOL – A DOUBLE BLINDED RANDOMIZED STUDY"** has been prepared by Dr. A. KARTHIK under my supervision in the Department of Anesthesiology, Government Kilpauk Medical College, Chennai during the academic period 2009-2012 and is being submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the University regulation for the award of Degree of Doctor of Medicine (M.D Anesthesiology) and his dissertation is a bonafide work.

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DECLARATION

I, Dr.A.Karthik, solemnly declare that the dissertation, **"COMPARISON OF POST CESAREAN ANALGESIA WITH EPIDURAL BUPIVACAINE-FENTANYL V/S BUPIVACAINE-NALBUPHINE V/S BUPIVACAINE-BUTORPHANOL – A DOUBLE BLINDED RANDOMIZED STUDY"** is a bonafide work done by me in the Department of Anesthesiology and Critical care, Government Kilpauk Medical College, Chennai under the guidance of Prof.Dr.P.S.Shanmugam, M.D.,D.A., Professor and HOD, Department of Anesthesiology, Government Kilpauk Medical College, Chennai.

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CONTENTS

Abstract

Study Objective

Comparison and study of post cesarean analgesia and side effect profile of epidural 0.125% bupivacaine-fentanyl v/s 0.125% bupivacaine-nalbuphine v/s 0.125% bupivacaine – butorphanol.

Design

Randomized, double-blinded study.

80 ASA physical status I and II women, aged 20-30 years, undergoing Elective Cesarean Section

Interventions

Patients were randomly allocated to four groups during the postoperative period to receive one of four epidural regimens: Group 1(NS): 10ml of 0.125% Bupivacaine + 1ml of Normal Saline; Group 2(FENT) 10ml of 0.125% Bupivacaine + 50ug of Fentanyl (1ml); Group 3(NALB) 10ml of 0.125% Bupivacaine + 5mg of Nalbuphine(0.5ml) +0.5ml of Normal saline to make it into 1ml; Group 4 (BUTOR): 10ml of 0.125% Bupivacaine + 1mg of Butorphanol (1ml)

Measurements

Onset and duration of analgesia were recorded. Hemodynamic variables, pain scores, sedation scores, and respiratory rate were monitored for 24 hours. Frequency and severity of respiratory depression, sedation, pruritus, nausea, and vomiting were recorded.

Main Results

The data of only 77 patients were included for calculation because 3 patients were dropped from the study as they had patchy sensory blockade to an extent of converting to GA. There was no statistically significant difference in demographic parameters.

The mean onset of analgesia and times to reach peak analgesia were significantly shorter while the mean durations of analgesia were significantly longer in the groups receiving fentanyl, nalbuphine & butorphanol than in the group receiving bupivacaine alone.

The *onset of analgesia* was earliest with Butorphanol group(3.42min) followed by fentanyl group(4.20min), Nalbuphine group(5.42min) & finally by control group(8.22min). The *duration of analgesia* was maximum with Butorphanol group (mean of 360min), followed by Fentanyl group (mean of 280min), Nalbuphine group (mean of 245) & control group (mean of 211min).

Satisfaction with the pain relief given was assessed by 1. Ability for independent side to side movement 2. VAS for satisfaction. It was observed that *satisfaction* was more with Butorphanol group followed by Nalbuphine group, Fentanyl group & by control group in the descending order.

Sedation was observed in all the groups (Control – 17%, Fentanyl – 25%, Nalbuphine – 58%, Butorphanol – 63%. Butorphanol & Nalbuphine groups had more incidence of sedation & higher grades of sedation (Grade 4)

Nausea & Vomiting was observed in both control group (incidence of 6%) & fentanyl group (incidence of 20%)

Pruritus was observed only in the fentanyl group with a incidence of 15%.

None of the patients developed hypotension, Bradycardia, respiratory depression.

Conclusions

Epidural 0.125% Bupivacaine combined with Butorphanol produces significantly earlier onset, longer duration and better quality of analgesia than 0.125% Bupivacaine - Nalbuphine combination / 0.125% Bupivacaine -Fentanyl combination / 0.125% Bupivacaine alone and is safe in parturients.

INTRODUCTION

The perioperative period is associated with a variety of pathophysiologic responses that may be initiated or maintained by nociceptive input. Although these responses may have had a beneficial teleologic purpose, the same response to the iatrogenic nature of modern-day surgery may be harmful. Uncontrolled perioperative pain may potentiate some of these perioperative pathophysiologies and increase patient morbidity and mortality. Hence Postoperative pain relief is very essential in improving perioperative care & hence quality of health care given to the patient.

The concept of opiate receptor subtypes (mu1 & mu2, kappa and sigma) and the advent of drugs with receptor-specific agonist and antagonist properties have further expanded the role of epidural opioids for intraoperative, postoperative, and obstetrical uses. Such opioids in combination with Local Anaesthetics are not only valuable in providing good analgesia, but also prolongs the duration of analgesia. Fentanyl, a synthetic opioid is a pure mu receptor agonist, and is highly lipid soluble. The mu receptor agonism leads to various side effects such as respiratory depression, nausea, vomiting, reduced GI motility, sedation & physical dependence. Hence the need of opioids with lesser side effects, but with good analgesic properties, led us to consider opioids agonist-antagonist –

Butorphanol & Nalbuphine as additives to local anaesthetic (via epidural route) for postcesarean analgesia.

Butorphanol, a synthetic opioid, is a strong kappa receptor agonist, a weak mu - receptor agonist/antagonist, and is relatively lipid soluble. Nalbuphine, a synthetic mu-receptor antagonist, kappa-receptor agonist opioid, is structurally related to the pure opioid agonist oxymorphone and the pure opioid antagonist naloxone. The antagonism at mu receptor (in case of Butorphanol & Nalbuphine) causes reduction in side effects such as nausea/vomiting, respiratory depression & pruritus. For these reasons, the use of epidural butorphanol / Nalbuphine in combination with 0.125% Bupivacaine for post-Caesarean section analgesia should produce less respiratory depression and a reduced incidence of these side effects compared with other opioid-Local Anaesthetic combination. The purpose of this study was to evaluate and compare the duration of analgesia and the side effect profiles of equipotent doses of fentanyl (pure agonist)/ Nalbuphine (agonist-antagonist)/ and Butorphanol (agonist-antagonist) given epidurally along with Local Anaesthetic mixture (0.125% bupivacaine), in the postoperative period for elective cesarean section.

REVIEW OF LITERATURE

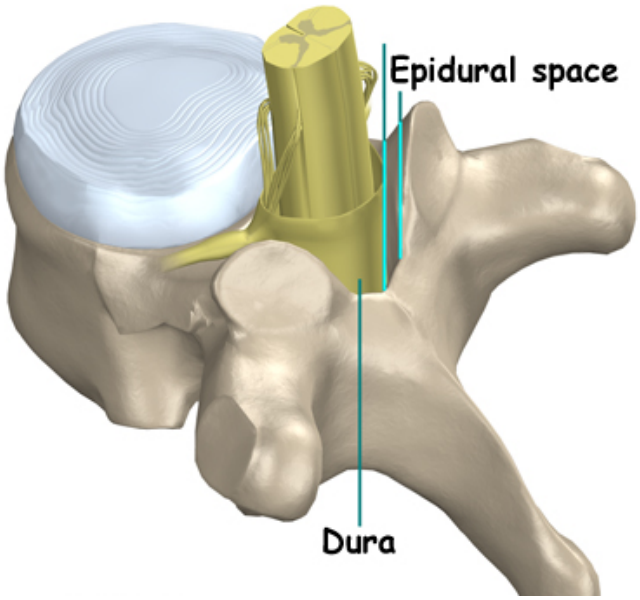
1. EPIDURAL ANATOMY & PHYSIOLOGY
2. EPIDURAL ANAESTHESIA & ANALGESIA
3. OPIOID PHARMACOLOGY
4. EPIDURAL OPIOIDS
5. POST CESAREAN ANALGESIA
6. EFFECTS OF EPIDURAL ANAESTHESIA & OPIOIDS ON BREAST FEEDING
7. VISUAL ANALOGUE SCALE (VAS)
8. STUDY REVIEWS

1. EPIDURAL ANATOMY AND PHYSIOLOGY

Anatomy of the Epidural space:

The epidural space surrounds the dural sac and is bounded by the posterior longitudinal ligament anteriorly, the ligamenta flava and the periosteum of the laminae posteriorly, and the pedicles of the spinal column and the intervertebral foramina containing their neural elements laterally. The space communicates freely with the paravertebral space through the intervertebral foramina. Superiorly, the space is anatomically closed at the foramen magnum where the spinal dura attaches with the endosteal dura of the cranium. Caudally, the epidural space ends at the sacral hiatus which is closed by the sacrococcygeal ligament. The

epidural space contains loose areolar connective tissue, semiliquid fat, lymphatics, arteries, an extensive plexus of veins, and the spinal nerve roots as they exit the dural sac and pass through the intervertebral foramina.

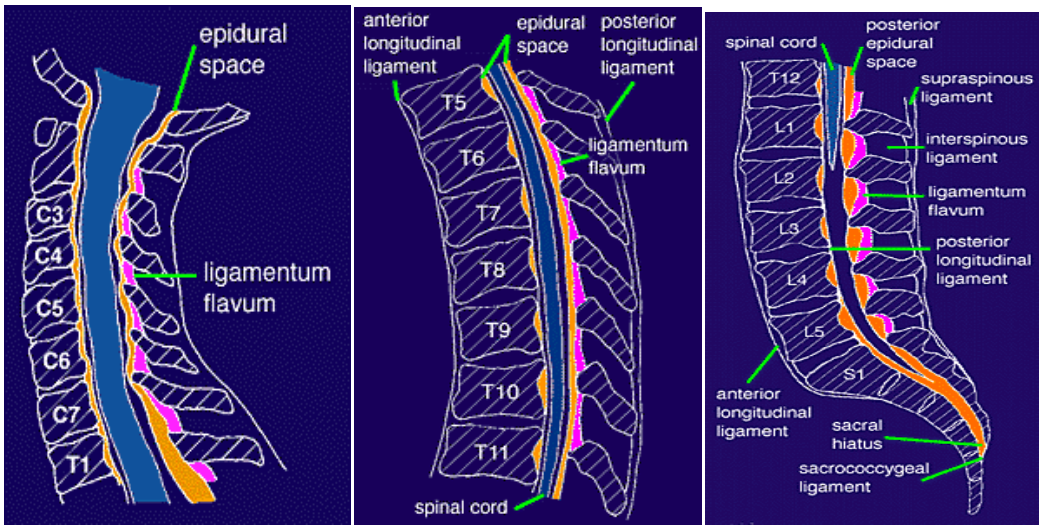


The *lumbar epidural space* in adults is segmented and discontinuous.

Areas of epidural fat under the ligamentum flavum extend under the laminae but are separated by areas where the posterior dura contacts, but does not adhere to, the periosteum of the lamina. This segmentation may impede the passage of an epidural catheter and promote coiling and misplacement. The anteroposterior dimension of the posterior space is greatest in the lumbar region and averages 5.0 - 6.0 mm in adult males.

The posterior epidural space becomes more continuous in the *thoracic region*. In the thoracic region the anteroposterior dimension of the posterior epidural space decreases but the space becomes more continuous. A thin layer of epidural fat extends between the lamina and the dura . Epidural catheters placed thoracically may pass easier because areas where the dura meets bone are fewer.

In more *cephalad cervicothoracic region*, the epidural fat disappears and the dura directly contacts lamina. The shallow space provides little room for excessive needle advancement. A homogenous semifluid fat pad free of vessels or fibrous septation occupies the posterior epidural space.



Presence of Dorsomedian ligamentous strands that extend from the ventral side of the vertebral arch and draw the dura posteriorly in a dorsomedian dural fold, the plica mediana dorasalis divides the posterior

epidural space into lateral compartments and narrows the space in the midline. Investigators have proposed that this segmentation of the epidural space may occasionally impede epidural catheter placement, or cause maldistribution of local anesthetics and unilateral or patchy anesthesia.

The open intervertebral foramina transmits intrabdominal pressure directly to the epidural space. Degenerative joint disease and aging can narrow the intervertebral foramina and prevent the spread of local anesthetic out of the foramina, resulting in greater longitudinal spread of local anesthetics in the epidural space.

A rich venous plexus almost entirely fills the anterior epidural space. The anterior dura adheres tightly to the posterior longitudinal ligament, which stretches across the intervertebral discs to form the anterior epidural space between the posterior longitudinal ligament & periosteum of the vertebral body.

As the size of the dural sac relative to the epidural space decreases at the L4-L5 level, the posterior longitudinal ligament falls away from the anterior dura, and fat fills the anterior epidural space. The increasing amounts of epidural fat anteriorly may contribute to the long latency of epidural anaesthesia typically observed in the L5 and S1 nerve roots.

The epidural venous plexus is a valveless system that communicates with the basivertebral vein, the intracranial sigmoid, occipital, and basilar venous sinuses, and the azygous system. Drugs, air, or other material injected into the epidural space can potentially reach the heart or brain directly through this route. Abdominal and thoracic veins connect with the venous plexus through the intervertebral foramina, and transmit intraabdominal and intrathoracic pressure to the epidural space.

Epidural space in pregnancy

Chronically increased intraabdominal pressure or obstruction of the IVC can distend the epidural venous plexus, with important implications for epidural anesthesia. This increases the risk of intravascular cannulation with an epidural catheter. It also effectively decreases epidural space volume, allowing local anesthetics to distribute more widely with resulting greater degrees of block. Exposure to greater vascular surface area also potentially increases the risk for local anesthetic toxicity due to absorption from the epidural space.

Physiological Effects of Epidural Blockade

The segmental nerves in the thoracic and lumbar region contain somatic sensory, motor and autonomic (sympathetic) nerve fibres. Sensory and autonomic fibres have a smaller diameter and are more easily blocked than larger, more rapidly-conducting motor fibres.

Effects on organ systems

Cardiovascular system. Vasodilatation of resistance and capacitance vessels occurs, causing relative hypovolaemia and tachycardia, with a resultant drop in blood pressure. This is exacerbated by blockade of the sympathetic nerve supply to the adrenal glands, preventing the release of catecholamines. If blockade is as high as T2, cardioaccelarator fibres are blocked and may lead to bradycardia. The overall result may be inadequate perfusion of vital organs and measures are required to restore the blood pressure and cardiac output, such as fluid administration and the use of vasoconstrictors.

Respiratory system. Usually unaffected unless blockade is high enough to affect intercostal muscle nerve supply (thoracic nerve roots) leading to reliance on diaphragmatic breathing alone. This is likely to cause distress to the patient, as they may feel unable to breathe adequately.

Gastrointestinal system. Blockade of sympathetic outflow (T5-L1) to the GI tract leads to predominance of parasympathetic (vagus and sacral parasympathetic outflow), leading to active peristalsis and relaxed sphincters, and a small, contracted gut, which enhances surgical access.

Endocrine system. Nerve supply to the adrenals is blocked leading to a reduction in the release of catecholamines.

Genitourinary tract. Urinary retention is a common problem with epidural anaesthesia. A severe drop in blood pressure may affect glomerular filtration in the kidney if sympathetic blockade extends high enough to cause significant vasodilation.

2. EPIDURAL ANAESTHESIA & ANALGESIA

Epidural anaesthesia is a central neuraxial block technique which provides segmental blockade. The epidural space was first described by Corning in 1901, and Fidel Pages first used epidural anaesthesia in humans in 1921. In 1945 Tuohy introduced the needle which is still most commonly used for epidural anaesthesia. Improvements in equipment, drugs and technique have made it a popular and versatile anaesthetic technique, with applications in surgery, obstetrics and pain control. Its versatility means it can be used as an anaesthetic, as an analgesic adjuvant to general anaesthesia and for postoperative analgesia in procedures involving the lower limbs, perineum, pelvis, abdomen and thorax.

Indications

General

Epidural anaesthesia can be used as sole anaesthetic for procedures involving the lower limbs, pelvis, perineum and lower abdomen. It is possible to perform upper abdominal and thoracic procedures under

epidural anaesthesia alone, but the height of block required, with its attendant side effects, make it difficult to avoid significant patient discomfort and risk. The advantage of epidural over spinal anaesthesia is the ability to maintain continuous anaesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration. This feature also enables the use of this technique into the postoperative period for analgesia, using lower concentrations of local anaesthetic drugs or in combination with different agents.

Specific uses

Hip and knee surgery. Internal fixation of a fractured hip is associated with less blood loss when central neuraxial block is used. The rate of deep venous thrombosis is reduced in patients undergoing total hip and knee replacement, when epidural anaesthesia is used.

Vascular reconstruction of the lower limbs. Epidural anaesthesia improves distal blood flow in patients undergoing arterial reconstruction surgery.

Amputation. Patients given epidural anaesthesia 48-72 hours prior to lower limb amputation may have a lower incidence of phantom limb pain following surgery

Thoracic trauma with rib or sternum fractures. Adequate analgesia in patients with thoracic trauma improves respiratory function

by allowing the patient to breathe adequately, cough and cooperate with chest physiotherapy.

Obstetrics. Epidural analgesia is indicated in obstetric patients in difficult or high-risk labour, e.g. breech, twin pregnancy, pre-eclampsia and prolonged labour. Furthermore, Caesarean section performed under central neuraxial block is associated with a lower maternal mortality and better perioperative period

Epidural anaesthesia for LSCS

When flexibility is necessary, epidural catheter technique is often chosen. In addition, women with an indwelling epidural catheter for labour who require CS usually receive the local anaesthetics through that catheter. The ideal anaesthetics should provide rapid onset of sensory block with an appropriate duration of action. The most commonly used local anaesthetics in this setting are 2% lignocaine 10-20ml (with or without adrenaline 1:200 000) or 0.5% bupivacaine 10-20ml. The latter has a longer duration of action, but a slower onset compared with lignocaine. Local anaesthetic requirements are less in pregnant patients. Proposed mechanisms include hormone-related changes in the action of spinal cord neurotransmitters, potentiation of the analgesic effect of endogenous analgesic systems, increased permeability of the neural sheath or other pharmacokinetic / dynamic differences. Hence large volume of local anaesthetic administered may be toxic & hence to

reduce the risk of toxicity the drug should be administered in fractionated doses.

Factors Affecting Epidural Anaesthesia

Site of injection After lumbar injection, analgesia spreads both caudally and, to a greater extent, cranially, with a delay at the L5 and S1 segments, due to the large size of these nerve roots. After thoracic injection, analgesia spreads evenly from the site of injection. The upper thoracic and lower cervical roots are resistant to blockade due to their larger size. The epidural space in the thoracic region is usually smaller and a lower volume of local anaesthetic is needed.

Dosage The dose required for analgesia or anaesthesia is determined by several factors but generally, 1-2ml of local anaesthetic is needed per segment to be blocked. The spread of local anaesthetic in the epidural space is unpredictable as the size of the epidural space is variable, as is the amount of local anaesthetic that leaks into the paravertebral space.

The dose (in milligrams) is a function of the volume injected and the concentration of the solution. It is important to remember that sympathetic nerve fibres have the smallest diameter and are most easily blocked , even with low concentrations of local anaesthetic. With an

epidural catheter, incremental dosing is possible and this is important in preventing excessively high sympathetic block with hypotension.

A useful concept is the "time to two-segment regression". This is the time from injection of the first dose of local anaesthetic to the point where maximum sensory level has receded by two segments. When two-segment regression has occurred, approximately one half of the original dose should be injected to maintain the block. The time to two-segment regression for lignocaine is 90-150 minutes, and for bupivacaine it is 200-260 minutes.

Age, height & weight There is an age related decrease in the volume of local anaesthetic needed to achieve a given level of block, presumably due to a decrease in the size and compliance of the epidural space. The patient's height appears to correlate to some extent with the volume of local anaesthetic needed. The safest approach is to inject incremental doses and monitor the effect carefully. There is little correlation between the weight of a patient and the volume of local anaesthetic needed, although in morbidly obese patients the epidural space may be compressed due to the effect on intra-abdominal pressure, and a smaller volume of local anaesthetic is needed. Furthermore, venous engorgement of the epidural space due to compression of the azygos venous system may further reduce the volume of the epidural space & increase the risk of puncture of an epidural vein.

Vasoconstrictor With bupivacaine, the addition of adrenaline has not been shown to prolong anaesthesia, while with lignocaine; the addition of adrenaline (usually 1:200 000) does prolong the duration of action. However, vasoconstriction does reduce the amount of systemic absorption of local anaesthetic drugs, and reduces the risk of toxicity.

Alkalinisation of local anaesthetics Commercially available solutions of local anaesthetics have a pH between 3.5 and 5.5, for chemical stability and bacteriostasis. Most local anaesthetics are weak bases and exist in their ionised (hydrophilic) form at this pH. Since nerve blockade is dependent on penetration of the lipid nerve cell membranes, and the non-ionised (lipophilic) form crosses membranes more easily, it follows that raising the pH of the solution will increase the proportion of drug in the non-ionised form and thus enhance nerve membrane penetration and speed up the onset of blockade. The addition of 8.4% sodium bicarbonate (0.5ml per 10ml of local anaesthetic solution) has become popular in achieving more rapid onset of blockade, for example, emergency Caesarean Section.

Epidural Management and Choice of Drugs

Once a catheter is placed, the filter and its connector are attached to the proximal end of the catheter. At this point, a test dose of local anaesthetic is injected to ensure that the catheter is not in the subarachnoid space. A small dose, e.g. 0.5% bupivacaine 3.5ml, bearing

in mind the volume of the filter, which is about 1ml, is injected and the response noted over the next few minutes. This dose, if injected into the subarachnoid space, will cause complete surgical anaesthesia below the level of injection, and will be accompanied by the drop in blood pressure usually seen in spinal anaesthesia. It is unlikely to cause significant sensory block or hypotension if correctly injected into the epidural space. Following the test dose, the procedure for the administration of further local anaesthetic will depend on the purpose of the epidural. The important principle is that any bolus injection of local anaesthetic should be given incrementally, and the response carefully monitored, so that the practitioner can react promptly to any adverse reaction. Once a satisfactory block is established, whether for surgical anaesthesia, analgesia in labour or any other indication, the block can be maintained either by intermittent bolus administration of local anaesthetic (with or without opioids) or as a continuous infusion, if the necessary equipment is available.

Epidural analgesia:

The use of epidural analgesia for pain relief was revolutionized by the use of epidural opioids after the discovery of opioid receptors in the dorsal horn of the spinal cord. Opioids have both presynaptic and postsynaptic effects in the dorsal horn and affect the modulation of nociceptive input but do not cause motor or sympathetic blockade.

Analgesia occurs by way of a spinal mechanism (diffusion of drug into the spinal fluid) and through supraspinal mechanism after systemic absorption.

Low concentration local anaesthetics, opioids, or combinations of both are effective in the control of postoperative pain in patients undergoing abdominal and thoracic procedures. Epidural analgesia has been shown to minimize the effects of surgery on cardiopulmonary reserve, i.e. diaphragmatic splinting and the inability to cough adequately, in patients with compromised respiratory function, such as those with chronic obstructive airway disease, morbid obesity and in the elderly. Epidural analgesia allows earlier mobilization, reduces the risk of deep venous thrombosis, and allows better cooperation with chest physiotherapy, preventing chest infections.

Advantages of Regional compared to GA for LSCS:

Ability to extend height and duration of block, Low frequency and slower onset of hypotension, Avoid tracheal intubation difficulty, Minimal risk of gastric aspiration, decreased blood loss, Avoidance of intentional dural puncture, Post-operative analgesia, positive breast feeding influences, Minimal newborn depression, Avoid hangover effects of G.A, early bowel recovery after surgery & early ambulation.

Disadvantages:

Patchy anaesthesia, Slow onset, No intense block, Accidental dural puncture & PDPH, Accidental i.v. injection, epidural hematoma,

Catheter misplaced into the subarachnoid space - a total spinal (can occur), Neurological injury lasting less than 1 year (rare, about 1 in 6,700), Epidural abscess formation (very rare, about 1 in 145,000). Neurological injury lasting longer than 1 year (extremely rare, about 1 in 240,000)

3. OPIOID PHARMACOLOGY:

Opioid receptor types

It is generally agreed that there are three major classes of receptors mediating opioid-induced analgesia. These are the mu-(1 & 2), kappa, and delta-opioid receptors . They are all blockable by naloxone an opioid receptor-specific competitive antagonist. There is also a receptor which binds opioids in a non-naloxone reversible fashion, referred to as the sigma opioid receptor, and it has no apparent role in mediating opioid-induced analgesia. It may mediate the psychotomimetic effects of some opioids, apparently related to its ability to bind phencyclidine.

CLASSIFICATION:

Classification of Opioid Compounds
Naturally Occurring
Morphine
Codeine
Papaverine
Thebaine
Semisynthetic
Heroin
Dihydromorphone/morphinone
Thebaine derivatives (e.g., etorphine, buprenorphine)
Synthetic
Morphinan series (e.g., levorphanol, butorphanol)
Diphenylpropylamine series (e.g., methadone)
Benzomorphan series (e.g., pentazocine)
Phenylpiperidine series (e.g., meperidine, fentanyl, sufentanil, alfentanil, remifentanil)

Mechanism of Analgesia

Pain control by opioids needs to be considered in the context of brain circuits modulating analgesia and the functions of the various types of receptors in these circuits. The analgesic effects of opioids arise from their ability to directly inhibit ascending transmission of nociceptive information from the spinal cord dorsal horn and to activate pain control circuits that descend from the midbrain, via the rostral ventromedial medulla (RVM), to the spinal cord dorsal horn. The μ-receptor produces analgesia within descending pain control circuits, at least in part by the removal of GABAergic (transmitting or secreting γ-aminobutyric acid) inhibition of RVM-projecting neurons in the PAG and spinally projecting neurons in the RVM. The actions of μ-receptor agonists are invariably analgesic, whereas those of κ-receptor agonists can be either analgesic or antianalgesic. The pain-modulating effects of κ-receptor agonists in the brainstem appear to oppose those of μ-receptor agonists.

Local spinal mechanisms, in addition to descending inhibition, underlie the analgesic action of opioids. In the spinal cord, opioids act at synapses either presynaptically or postsynaptically. Opioid receptors are abundantly expressed in the substantia gelatinosa, where release of substance P from the primary sensory neuron is inhibited by opioids.

The actions of opioids in the bulbospinal pathways are critical to their analgesic efficacy. Opioid actions in the forebrain clearly contribute

to analgesia because decerebration prevents analgesia when rats are tested for pain sensitivity with the formalin test and microinjection of opioids into several forebrain regions is analgesic in this test.

	μ	**δ**	**κ**
Analgesia Supraspinal Spinal Peripheral	 +++ ++ ++	 - ++ -	 - + ++
Respiratory depression	+++	++	-
Pupil constriction	++	-	+
Reduced GI motility	++	++	+
Euphoria	+++	-	-
Dysphoria	-	-	+++
Sedation	++	-	++
Physical dependence	+++	-	+

Mood Alteration

The mechanisms by which opioids produce euphoria, tranquility, and other alterations in mood (including rewarding properties) are not entirely clear. Behavioral and pharmacologic evidence points to the role of dopaminergic pathways, particularly those involving the nucleus accumbens. The locus ceruleus contains both noradrenergic neurons and high concentrations of opioid receptors and is postulated to play a critical

role in feelings of alarm, panic, fear, and anxiety. Neural activity in the locus ceruleus is inhibited by both exogenous opioids and endogenous opioid peptides.

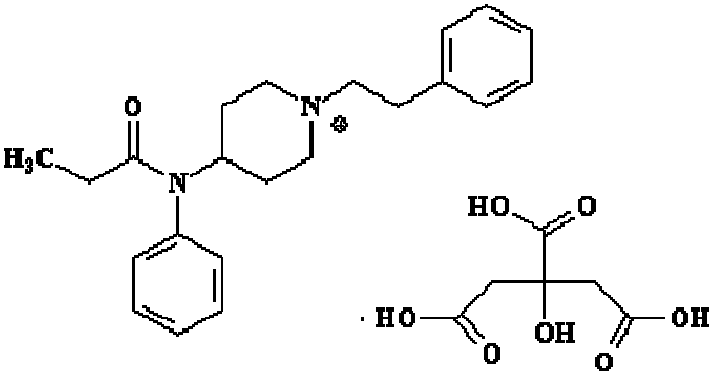
Compound	**Major Receptor Types**		
	Mu	**κ**	**δ***
AGONIST			
Morphine (and codeine, oxycodone, meperidine, hydromorphone,)	Ag	Ag	
AGONISTS-ANTAGONISTS			
Buprenorphine	pAg	Ant	Ant
Pentazocine	pAg	Ag	
Nalbuphine	pAg	Ag	
Butorphanol	pAg	Ag	
ANTAGONISTS			
Naloxone	Ant	Ant	Ant
Naltrexone	Ant	Ant	Ant
Underlined item indicates predominant receptor effects			

Drug	Analgesia	Respiratory Depression	Antitussive Effect	Constipation	Dependence Liability
MIXED OPIOID AGONIST-ANTAGONISTS					
buprenorphine	+++	++	+	++	+
butorphanol	+++	++	0	+	+
nalbuphine	+++	++	0	+	+
Pentazocine	+++	++	0	+	+
OPIOID ANTAGONISTS					
naloxone	0	0	0	0	0
naltrexone	0	0	0	0	0
*Ratings range from none (0) to high (++++)					

	Equianalgesic Potent dose	Duration of Analgesia (hr)
Morphine	10mg	4-5
Buprenorphine	0.3-0.4mg	>6
Butorphanol	2mg	3-4
Nalbuphine	10mg	3-6
Fentanyl	100ug	1

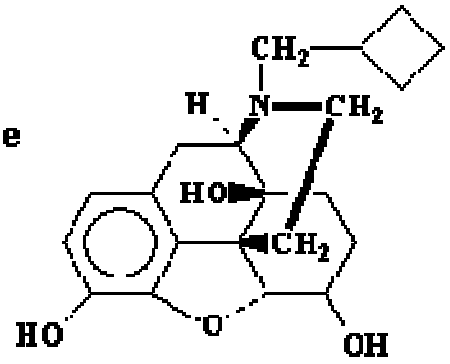
Fentanyl Citrate

$C_{22}H_{28}N_2O \cdot C_6H_8O_7$



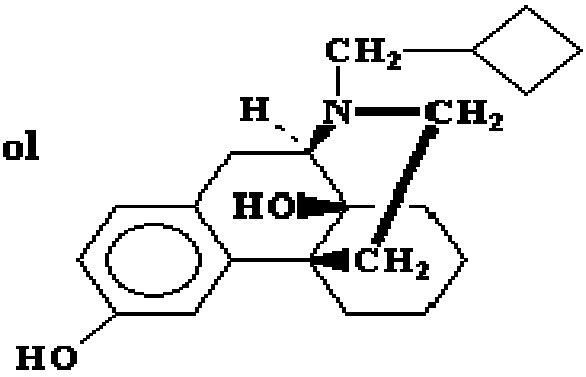
Nalbuphine Hydrochloride

$C_{21}H_{27}NO_4$



Butorphanol

$C_{21}H_{29}NO_2$



Fentanyl

First synthesized in Belgium in late 1950 s. Introduced in medical practice in 1960 s as an intravenous anaesthetic agent. It is a phenylpiperidine derivative acts as a pure agonist at mu opioid receptors. 100 times more potent than morphine. Structurally related to meperidine.

Pharmacokinetics - Effect site equilibration time (b/w blood & brain) is 6 min. It is highly lipid soluble. Rapid redistribution 75% of initial dose undergoes first pass pulmonary uptake. N-Demethylation produces norfentanyl(main metabolite), which begins to appear in plasma as early as 1.5 minutes after injection & is excreted by kidneys. Highly protein bound (79%-87%) and significant amounts (40%) are taken up by RBCs.

The plasma concentration of fentanyl required for postoperative analgesia was approximately 1.5 ng/mL, but levels of at least 2 to 3 ng/mL are usually required during surgery if the only inhaled agent is N_2O.

Preparations: Available as Intravenous injection, Transdermal patch(duragesic), Oral transmucosal fentanyl citrate(otfc), Push button fentanyl

Uses : Analgesia - Intravenous boluses of fentanyl (1 to 3 μg/kg), Infusion rates range from 0.01 to 0.05 μg/kg/min for fentanyl . In doses 2-10microg/kg iv to blunt circulatory responses to laryngoscopy or surgical stimulation. Large doses 25-50microg/kg for opioid induction in cardiac surgeries.

Side effects: Repeated doses or continuous infusions of fentanyl are most likely to result in significant depression of spontaneous

ventilation, nausea & vomiting, pruritus, chest wall rigidity (which can be attenuated by co- administration of induction agents like Thiopentone & Muscle relaxants in case of General Anaesthesia)

Nalbuphine

Nalbuphine is an agonist-antagonist opioid that is structurally related to oxymorphone and naloxone and binds to μ-receptors, as well as to κ- and δ-receptors. Nalbuphine acts as an antagonist at the μ-receptor and as an agonist at the κ-receptor. Activation of supraspinal and spinal κ-receptors results in limited analgesia, respiratory depression, and sedation. Nalbuphine, like other agonist-antagonist compounds, interferes with the analgesia produced by pure μ-agonists.

Mark W. Gunion et al - A key point in understanding the utility of nalbuphine is that while it binds readily to both the mu- and kappa-receptors, its actions on these populations are divergent. When nalbuphine binds to mu-receptors it serves only to competitively displace other mu-agonists from the receptor, without itself displaying any agonist activity itself. At mu-receptors, then, nalbuphine has only antagonist effects, similar to those of naloxone. When nalbuphine binds to kappa-receptors, however, it has an agonist activating effect. This pattern of binding and effects defines nalbuphine as a mixed agonist—antagonist.

Pharmacokinetics: Equal in potency as an analgesic to morphine and ¼ as potent antagonist as nalorphine. Nalbuphine is available only for parenteral use. The onset of effect is rapid (5 to 10 minutes), and its duration is long (3 to 6 hours) because of an extended plasma elimination half-life (5 hours). Metabolised in the liver and has an elimination half-time of 3-6 hours. The pharmacokinetic profile of epidural nalbuphine was similar to that seen with iv injection.

Nalbuphine (10 mg) caused no significant changes in systemic, pulmonary arterial, and pulmonary capillary wedge pressure in patients experiencing myocardial infarction.

Uses : Nalbuphine has been administered as an analgesic supplement for conscious sedation or balanced anaesthesia and as an analgesic for postoperative and chronic pain problems. 10 mg IM produces analgesia, 10-20 mg IV reverses postoperative depression of ventilation caused by fentanyl but maintains analgesia . Premedication with nalbuphine (0.1 mg/kg) in patients scheduled for cardiac surgery results in sedation, relief of anxiety, and respiratory depression similar to morphine (0.1 mg/kg), but it causes no significant hemodynamic changes.

For postoperative patient-controlled epidural analgesia, the combination of hydromorphone, 0.075 mg/mL, and nalbuphine, 0.04 mg/mL, resulted in a lower incidence of nausea and decreased need for bladder catheterization when compared with hydromorphone alone.

The problem is that nalbuphine, like other mixed agonists—antagonists, exhibits a ceiling effect. That is, increasing doses of drug produce increasing intensity of analgesia only up to a point; beyond that point, further increases in dose do not result in increased intensity of analgesia[(1)].

Pugh GC et al – Br J Anaesth 1987;59:1356—63[(2)]

The use of the opioid mixed agonist—antagonist nalbuphine as an analgesic agent provides a number of advantages. Used as the sole opioid analgesic, it can satisfactorily cover mild to moderate pain with a low incidence of side effects. The ceiling effect of nalbuphine, which prevents it from supplying sufficient analgesia to cover the most severe discomfort, also prevents increasing sedation and respiratory depression as the dose is increased, potentially providing an increased safety margin in comparison to mu-agonists. When nalbuphine is used concurrently with mu-agonists (e.g. morphine, hydromorphone, fentanyl), the benefits of both mu- and kappa-analgesia can be obtained, with simultaneously decreased incidence and severity of the common mu-agonist side effects (pruritis, nausea/emesis, constipation, urinary retention, respiratory depression and undesirable sedation).

Side effects: Sedation, Dysphoria , Withdrawal symptoms

Butorphanol

Synthetically derived opioid agonist - antagonist analgesic of the phenanthrene series. Dose as expressed as the tartrate salt.1mg of salt is equivalent to 0.68mg of free base. Butorphanol is an agonist at κ-receptors. Its activity at μ-receptors is either antagonistic or partially agonistic.

Pharmacokinetics: Binds with plasma protein to the extent of 80%. Major metabolite is hydroxybutorphanol,while norbutorphanol is produced in small amount. It is available only in parenteral form. After intramuscular injection, the onset of effect is rapid, and peak analgesia occurs within 1 hour & the duration of action of butorphanol is similar to that of morphine, its plasma half-life is only 2 to 3 hours.

In healthy volunteers, butorphanol (0.03 or 0.06 mg/kg IV) produces no or minimal cardiovascular changes. However, in patients with cardiac disease, butorphanol causes significant increases in cardiac index, left ventricular end-diastolic pressure, and pulmonary artery pressure. Butorphanol is subjected to less abuse and has less addictive potential than morphine or fentanyl does. Acute biliary spasm can occur after butorphanol, but increases in biliary pressure are less than after equipotent doses of fentanyl or morphine.

Prepartation in Ampoules- 1mg /1 ml; 2mg /1 ml

Uses: Moderate to severe postoperative pain-1mg iv single dose and repeated every 3-4hr. Effective dose range is 0.5-2mg i.v or 2mg i.m (1-4mg), Preoperative or preanesthetic medication- 2mg i.m 60 minutes before surgery. Supplement to balanced anesthesia-2 mg i.v before induction or 0.5-1mg iv in increment doses, Relief of pre partum pain=1-2mg iv/i.m. Transnasal butorphanol is effective in relieving migraine and postoperative pain.

Side effects: Although butorphanol at dose of 10mg im causes as much respiratory depression as the same dose of morphine, higher doses reach a ceiling. Other side effects after butorphanol include drowsiness, sweating, nausea, and CNS stimulation.

4. EPIDURAL OPIOIDS/ LOCAL ANAESTHETICS

The addition of opioids to local anaesthetic solutions has gained popularity; as the opioids have a synergistic effect by acting directly on opioid receptors in the spinal cord. Various opioids, such as morphine (2-5mg), fentanyl (50-100mcg) and diamorphine (2-4mg), have been used successfully both alone and in combination with local anaesthetic drugs, during labour, for intraoperative use and for postoperative analgesia. The combination of low-concentration local anaesthetic and low-concentration mixtures of opioids, administered by slow infusion rather than as intermittent boluses has been shown to be very effective in the management of postoperative pain.

Pethidine 25-75mg, in particular, has a structure similar to local anaesthetics and is effective in providing surgical anaesthesia and postoperative analgesia.

Fentanyl is also used frequently in epidural 50-100ug along with Local Anaesthetics.

All opioids given by this route have the potential to cause respiratory depression, and this should be borne in mind when the patient is discharged from the care of the anaesthetist. Patients should be managed postoperatively in an area with monitored care.

Pharmacokinetics of epidural opioids

Side effects of intrathecal and epidural opioids are caused by presence of the drug in either CSF or blood. Therefore, following administration of intrathecal and epidural opioids, side effects will be profoundly affected by their pharmacokinetic behaviour. Fentanyl and sufentanil are, respectively, approximately 800 and 1600 times as lipid-soluble as morphine. When administered intrathecally or epidurally, therefore, morphine will exhibit slower onset and longer duration of antinociception and a higher incidence of side effects. Fentanyl and sufentanil penetrate the spinal cord quickly, leaving little drug to ascend cephalad in cerebrospinal fluid. In contrast, morphine penetrates the

spinal cord slowly, allowing considerable amounts of drug to ascend cephalad in cerebrospinal fluid.

Following lumbar intrathecal morphine administration, appreciable cervical CSF concentrations occur one to five hours after injection, while cervical CSF concentrations of a highly lipophilic opioids, similarly administered, are minimal. CSF ascends in a cephalad direction from the lumbar region, reaching the cisterna magna by one or two hours and the fourth and lateral ventricles by three to six hours. Highly lipophilic opioids are removed from CSF rapidly secondary to vascular reabsorption and spinal cord penetration. In contrast, morphine persists in cerebrospinal fluid for prolonged periods and may depend on reabsorption through arachnoid granulations for elimination. The terminal elimination half-life of morphine in CSF is similar to that in plasma, two to four hours.

Following epidural administration, cerebrospinal fluid concentrations of fentanyl peak in 10 to 20 min while sufentanil concentrations peak in about six minutes and that of morphine, peak in one to four hours. Furthermore, only about 3% of the dose of morphine administered epidurally crosses the dura to enter cerebrospinal fluid.[3]

The epidural space contains an extensive venous plexus. Therefore, vascular reabsorption following epidural administration of opioids is extensive. Epidural administration of morphine, fentanyl, or

sufentanil produces opioid blood concentrations that are similar to an intramuscular injection of an equivalent dose. Following epidural administration, fentanyl blood concentrations peak at about five to ten minutes[4,5] while sufentanll blood concentrations peak even faster[6]. In contrast, blood concentrations of morphine following epidural administration peak at about 10 to 15 min.

Mark A. Chancy et al - Can J Anaesth 1995 / 42:I0 / [7]

Advantages of Intrathecal and epidural opioids produce profound segmental antinociception in doses much smaller than would be required for comparable antinociception if administered systemically. Antinociception may be prolonged; when morphine is utilized, it may persist for days following a single injection. Unlike the response to local anaesthetics, there is no motor, sensory, or autonomic blockade. Paralysis and hypotension, therefore, are absent. Another critical advantage over local anaesthetics is the availability of a specific opioid receptor antagonist, naloxone.

Cohen et al - Reg Anesth 1991;16:141–9[8]

Patients receiving IV patient-controlled analgesia and IM opioids report more severe pain after Cesarean section compared with those receiving intrathecal (IT) and epidural-administered opioids

Neuraxial opioids; side effects

Pruritus, Nausea and vomiting, Urinary retention, Respiratory depression

Mental status changes, Central nervous system excitation, Herpes simplex labialis virus reactivation, Neonatal respiratory depression, Ocular dysfunction, Gastrointestinal dysfunction, Anaphylaxis

Drug	Correlation of Respiratory Depression with Dose
Morphine	Increases proportionally with dose
Buprenorphine	Ceiling effect at 0.15-1.2 mg in adults
Butorphanol	Ceiling effect at 30-60 μg/kg
Nalbuphine	Ceiling effect at 30 mg in adults
Fentanyl	Increases proportionally with dose

A.D. Baxter et al: Can J Anaesth 1991 / 38:2[(9)]

Epidural opioids provide effective postoperative analgesia, but may have undesirable side-effects such as pruritus, urinary retention, nausea and vomiting, and most importantly respiratory depression[(10)]. The incidence of severe respiratory depression is low**,** but mild carbon dioxide

(CO2) retention and abnormal respiratory patterns are seen more frequently

5. POST CESAREAN ANALGESIA

Post-cesarean delivery pain relief is important. Good pain relief will improve mobility and can reduce the risk of thromboembolic disease, which is increased during pregnancy. Pain may also impair the mother's ability to optimally care for her infant in the immediate postpartum period and may adversely affect early interactions between mother and infant. Pain and anxiety may also reduce the ability of a mother to breast-feed effectively. It is necessary that pain relief be safe and effective, that it not interfere with the mother's ability to move around and care for her infant, and that it result in no adverse neonatal effects in breast-feeding women.

Systemic Administration:

Intramuscular/Subcutaneous Injection: IM or subcutaneous administration of opioids is the most frequently used modality for post-cesarean delivery pain relief. However, there are some limitations to their use. First, drug administration requires injection, often repeated, which may be uncomfortable for many women. Second, there is large inter-individual variability in opioid pharmacokinetics and drug requirements, hence some have effective pain relief but have an increased incidence of

unwanted effects, such as somnolence and sedation, whereas at smaller concentrations, pain relief may be inadequate.

Patient-Controlled IV Analgesia: The device is programmable for the dose administered, a lockout interval, whether a basal infusion of drug is given, and as an added protection, maximum dosages within specified time periods. The advantage of IVPCA is that it reduces the peaks and valleys in blood drug concentrations and pain relief observed in post-cesarean delivery women. Pain relief with IVPCA has been shown to be superior to conventional IM opioids for pain relief in women having had a cesarean delivery. The most significant limitations to the use of IVPCA in postpartum women relate to the device itself and patient ability to use it correctly.

Neuraxial Opioids:

Spinal: Mechanism of Action - Opioids administered in the subarachnoid space appear to act principally on mu receptors in the substantia gelatinosa of the dorsal horn by suppressing excitatory neuropeptide release from C fibers. The degree of uptake from the cerebrospinal fluid by the dorsal horn is determined primarily by the physicochemical properties of the drug, and in particular, lipid solubility.

Uptake of opioids into the systemic circulation after intrathecal injection is usually not significant, as the doses typically used in the

spinal space are small. This is particularly important to breast-feeding women and is an advantage of neuraxial modes of post-cesarean delivery pain relief as compared with the larger doses of opioids required systemically.

Epidural: Mechanicm of Action- a hydrophilic drug, such as morphine, is injected, it moves slowly across the arachnoid granulations there is a predominant spinal mechanism of analgesia after epidural administration of the drug. Epidural fentanyl most probably acts at both supraspinal (via systemic delivery) and spinal sites, in addition to drug diffusing to spinal receptors from the cerebrospinal fluid.

NSAIDs: Pain after cesarean delivery may have at least two components: postoperative (somatic) pain from the wound itself and visceral pain arising from the uterus. Although somatic pain may be relieved by opioids, visceral pain may be more difficult to treat. NSAIDs are effective for relieving pain related to menstrual cramping and, as a result, there has been interest in the use of NSAIDs to treat a component of pain after cesarean delivery. Unfortunately, NSAIDs alone are insufficient to effectively treat post-cesarean delivery pain. However, inclusion of NSAIDs in a multimodal approach to pain relief after cesarean delivery has been very successful both in improving the quality of analgesia resulting from systemic or neuraxially administered opioids and reducing side effects. For instance, use of IM diclofenac 75 mg

results in a morphine-sparing effect and a decrease in side effects related to morphine use. The disadvantages to using NSAIDs relate to the potential for gastrointestinal side effects and platelet dysfunction. Also COX 2 inhibitors may have a tocolytic action on the uterus and hence avoided.

New Drugs, New Delivery Systems

Clonidine: Clonidine exerts its antinociceptive effect by stimulating the alpha 2 adrenergic receptor and modulating pain pathways in the dorsal horn . It is effective for both somatic and visceral pain. The addition of clonidine (up to 100 ug) alone to spinal local anesthetic for post-cesarean delivery analgesia has found to cause unacceptable degree of hypotension, bradycardia, nausea and vomiting. In another study, adding clonidine, 75 or 150 ug, to epidural morphine, 2 mg, prolonged the duration of analgesia after cesarean delivery from a mean +/- sd of 6.27 +/- 1.6 h with morphine alone to 13.25 +/- 3.8 h with clonidine 75ug and 21.55+/- 6.3 h with clonidine 150ug , with the combination, without incurring additional side effects[(11)]. A black box warning exists prescribing the use of clonidine (or other angiotensin converting enzyme inhibitors) during the second and third trimester because of the potential for fetal injury and death.

Dexmedetomidine: Dexmedetomidine is the other alpha 2 adrenergic receptor agonist that has recently been approved for iv use.

Like clonidine, it can cause somnolence, which is undesired in postpartum women, but, in general, respiratory variables, such as oxygen saturation and respiratory rate, are better maintained with dexmedetomidine than with parenterally administered opioids. Unfortunately, there is little experience with routine use of the drug in postpartum women. At this time, dexmedetomidine is not approved for neuraxial use[(12)]

Neostigmine: Neuraxial neostigmine produces analgesia by inhibiting degradation of acetylcholine in the spinal cord. Results of studies using neostigmine for postpartum pain relief have been disappointing because of side effects such as nausea, shivering, and sedation[(13)]**.**

Lipid-Encapsulated Morphine: Advances in technology have allowed for a sustained morphine delivery system to be used with epidural analgesia. Depo- Foam™ is a lipid-based vehicle consisting of aqueous chambers that encapsulate the active drug, such as morphine (DepoDur™), resulting in sustained release and prolonged analgesia when the drug is administered epidurally. In one study, unencapsulated morphine was compared with encapsulated morphine at doses of 5, 10, and 15 mg administered epidurally at time of cord clamp[(14)]. The encapsulated morphine resulted in superior analgesia of longer duration than the unencapsulated drug. There are two concerns that maylimit use

of the drug in obstetrics. First, the Depo- Foam™ vehicle may be lysed in the presence of local anesthetic, releasing a relatively large amount of morphine in the epidural space and risking respiratory depression; because of this concern, the label for DepoDur ™ is used.

6. EFFECT OF EPIDURAL & OPIOIDS ON BREAST FEEDING

Barton M et al - Aust Coll Midwives Inc J 1996;9:14 –9

Postoperative epidural analgesia has been associated with an improvement in the mother's ability to mobilize and interact with her newborn infant.

Hirose et al.[15] randomized 2 groups of 15 patients who underwent a cesarean delivery under spinal anaesthesia to receive either postoperative epidural analgesia with bupivacaine or IV analgesia. They found that mothers receiving epidural bupivacaine for 3 postoperative days experienced significantly lower pain scores and had more success with breast feeding and greater infant weight gain. In conclusion, it appears that early maternal-infant bonding leads to greater success in breast feeding as does adequate postoperative pain control. Thus, epidural anaesthesia is preferable to general anesthesia, and adequate postoperative analgesia is desirable.

Multiple investgations involving large numbers of patients have revealed that Intrathecal and epidural opioids are safe for the mother and neonate provided that conventional doses are used.

Butorphanol is considered effective and safe after cesarean delivery with minimal effect on the fetus, and the newborn. Further, the American Academy of Pediatrics Committee on Drugs has categorized butorphanol as compatible with breast feeding.[16]

Dose-response study of a combination of 0.25% bupivacaine combined with 0,1, 2, or 3 mg of butorphanol was studied in 40 laboring parturients. The optimal dose of butorphanol combined with 8.5 to 10 ml 0.25% bupivacaine was 2 mg. Adverse fetal effects were not observed except that of a low amplitude sinusoidal fetal heart rate pattern with doses of 3 mg butorphanol. All neonatal observations were normal. It is concluded that epidural butorphanol can be a useful and safe adjunct to bupivacaine used for epidural analgesia during labor[17]

Following administration of epidural fentanyl or epidural sufentanil to obstetric patients, breast milk conentration of opioid is negligible[18]. While the elimination half-life of nalbuphine in neonates is 4.1 hr, compared to 7-32hrs for pethidine. Thus, any fetal effects of transplacentally/ breast milk transferred opioid will be of shorter duration if nalbuphine is used for maternal analgesia, rather than meperidine[19]

7. VISUAL ANALOGUE SCALE

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured (example - the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain). From the patient's perspective this spectrum appears continuous and their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised.

Operationally a VAS is usually a horizontal line, 10cm/100 mm in length, anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in centimetres/ millimetres from the left hand end of the line to the point that the patient marks.

VAS score has linear scale properties (i.e., the difference in pain between each successive increment is equal)[20]. Thus, a VAS pain score of 6 cm indicates twice as much pain as a VAS score of 3cm, and the difference between a VAS score of 3 and 4cm would be of the same magnitude as the difference between VAS scores of 7and 8 cm.

Collins et al[21] concluded that a VAS score of at least 54mm could be equated with a rating of severe pain. The VAS is a unimodal measure of pain intensity and cannot adequately represent all aspects of pain perception. The extremes of pain—"no pain" and "worst pain ever"—may not truly represent absolute limits of perception. Despite these limitations, it remains a widely used, validated measure of pain. in postoperative patients with acute mild-to-moderate pain, the VAS score is a linear scale. Changes in the VAS score represent a relative change in the magnitude of pain sensation.

8. STUDY REVIEWS:

1. *Gambling et al* compared postcesarean outcomes of epidural morphine 4 mg plus epidural Butorphanol 3mg versus epidural morphine 4 mg alone. Patients receiving butorphanol in the study had significantly greater analgesia, a significantly lower incidence of treatment for pruritus, and significantly greater overall satisfaction compared with controls.

2. *Bernard Wiftels et al* – In this study saline or Butorphanol(BU) 1 or 3 mg was added to epidural morphine 4 mg for postcesarean analgesia, there was no difference in analgesic intensity or duration; however, parturients who received BU 3 mg had significantly less nausea and pruritus than the other two groups[22]. No patient complained of drowsiness, nor did nursing personnel observe a greater

incidence of sedation among parturients who had received epidural BU [22]. These results support the assumption that agonist-antagonist opioids are effective in preventing untoward opioid side effects.

3. *Carl rosow et al* - Epidural butorphanol has already shown some promise in obstetrics. A single dose provides relief of post Caesarean pain for six to ten hours without pruritus or excessive sedation.

4. *Quisqueya T. Palacios et al* - Anaesthesia for the Caesarean section (T4 sensory level) was produced with lidocaine, two per cent with 1:200,000 epinephrine, injected through an epidural catheter inserted in the L2_3 or L3-4 interspace.. The test medications were morphine, 5 mg, and butorphanol 1, 2, or 4 mg. The time to onset of epidural analgesia following butorphanol was more rapid than following morphine. 14, 22 and 17 per cent of patients treated with butorphanol 1,2 or 4 mg respectively, had not requested supplemental medication at eight hours, 65 per cent of the morphine patients had not been remedicated at eight hours. Pruritus occurred in only 1.4 per cent of the Butorphanol patients compared with 43 per cent of the morphine patients[23].

5. *Szabova A et al*- postoperative epidural butorphanol / bupivacaine with the gold-standard epidural analgesic infusion fentanyl / bupivacaine in children. Epidural butorphanol provided similar analgesia to epidural fentanyl after urological procedures in children, but butorphanol caused less pruritus than fentanyl. Epidural analgesia with

butorphanol/bupivacaine is effective in children undergoing urological procedures. When compared with epidural fentanyl, epidural butorphanol causes significantly less itching.

6. *J S Naulty et al* (Anaesthesiology v81, sep 1994) Epidural Butorphanol after delivery of baby 1mg, 2mg, 4mg, results showed increasing duration of analgesia as dose increases, but no statistical significance. No case reported pruritus. 80% of cases reported somnolence.

7. *Baxter AD et al* - Can J Anaesth 1991;38:175-82. Nalbuphine (NB) is a mixed agonist-antagonist opioids with only modest analgesic properties after epidural administration. After cesarean delivery with epidural lidocaine, epidural NB in doses of 10,20, and 30 mg promoted satisfactory analgesia, but with a duration of only 1-3 h[(24)]

8. *Weksler and Ovadia et al* administered 0.15 mg/kg nalbuphine epidurally to 30 patients following upper abdominal surgery, which produced a mean duration of analgesia of 6.5 hr.[(25)] following upper abdominal surgery, which produced a mean duration of analgesia of 6.5 hr. Somnolcence was the only bothersome side-effect, occurring in 55% of the patients; however, no patient developed respiratory depression as measured by sequential arterial PaCO2 measurements for 24 hr.

9. *McMorland et al* reported only fair and inconsistent analgesia following epidural Nalbuphine (dose range 5-20 mg) after Caesarean delivery in 40 patients. Side-effects were minimal and the respiratory response to a CO2 challenge at three and six hours after epidural opioid was unaffected.

10. Thoracic epidural nalbuphine (0.075-0.3 mg.kg -I) has been found by *Baxter et al.* to be an ineffective analgesic for post-thoracotomy patients**.** These authors found no evidence of a dose-response effect in the nalbuphine dose-range studied. Moreover, the pharmacokinetic profile of epidural nalbuphine was similar to that seen with iv injection**(26).**

11. *Culebras X et al* - 2000-09, Anesth Analg., 91(3):601-5. Intrathecal nalbuphine, at three different doses, and intrathecal morphine for postoperative pain relief after cesarean deliveries. Ninety healthy patients at full term who were scheduled for elective cesarean delivery with spinal anaesthesia were enrolled in the study. They received 10 mg of hyperbaric bupivacaine 0.5% with either morphine 0.2 mg (Group 1), nalbuphine 0.2 mg (Group 2), nalbuphine 0. 8 mg (Group 3), or nalbuphine 1.6 mg (Group 4). Postoperative analgesia lasted significantly longer in the morphine group, compared with the nalbuphine groups (P: < 0.0001). In the nalbuphine groups, postoperative analgesia lasted longest with the 0.8-mg dose. The additional increase to 1.6 mg did not increase efficacy. The incidence of pruritus was significantly higher

in Group 1 (11 of 22), compared with Group 2 (0 of 22, P: < 0.0002), Group 3 (0 of 23, P: < 0.0001), and Group 4 (3 of 20, P: < 0.02). Postoperative nausea and vomiting were more frequent in Group 1 (5 of 22), compared with Group 2 (0 of 22, P: < 0.05), Group 3 (0 of 23, P: < 0.05), and Group 4 (3 of 23, not significant). There was no maternal or newborn respiratory depression. Neonatal conditions (Apgar scores and umbilical vein and artery blood gas values) were similar for all groups. This study suggests that intrathecal nalbuphine 0.8 mg provides good intraoperative and early postoperative analgesia without side effects. However, only morphine provides long-lasting analgesia but with unwanted side effects.

12. *Camann WR et al* - 1991-09, Can J Anaesth., 38(6):728-32. Epidural Anaesthesia with local anaesthetics – Lignocaine & Chlorprocaine was carried out, and postoperatively the effect of Nalbuphine in doses of 10mg, 20mg & 30mg were studied. The results of this study suggests that epidural nalbuphine (20 or 30 mg) provides only two to four hours of effective analgesia following Caesarean delivery, and then only in the presence of some degree of residual lidocaine anaesthesia. When 2-CP was used as the primary local anaesthetic agent, postoperative epidural nalbuphine (regardless of dose) failed to provide any analgesic effects in the absence of residual local anaesthetic block **(27).**

13. *Orawan Pongraweewan et al* (J Med Assoc Thai 2009; 92 (6): 782-6) purpose of the study was to test the clinical efficacy of epidural nalbuphine 5 mg and 10 mg for prevention of morphine-induced pruritus. Epidural Nalbuphine 10 mg reduced the incidence of pruritus for 6 h was the conclusion.

14. *Wittles et al* found that epidural nalbuphine 10 mg reduced the incidence of pruritus from 48% to 20% for 6 h[(28)]

15. *Hunt et al.* conducted a randomized study that demonstrated a dose-dependent increase in postcesarean delivery analgesia up to a fentanyl dose of 6.25 ug, beyond which there was no added advantage. Furthermore, mean duration of effective analgesia was only 200 min.

AIM OF THE STUDY

Comparison and study of post cesarean analgesia and side effect profile of epidural 0.125% bupivacaine-fentanyl v/s 0.125% bupivacaine-nalbuphine v/s 0.125% bupivacaine – butorphanol.

METHODOLOGY

After getting Ethical committee approval, 80 parturients belonging to ASA physical status I & II undergoing Elective LSCS were enrolled.

INCLUSION CRITERIA

ASA Class I & II

Elective cesarean section

EXCLUSION CRITERIA

ASA Class III & IV (Severe PIH, Stenotic Valvular Heart disease) Emergency Surgery (Includes Fetal distress, threatened rupture, hemodynamic compromise).

Not willing for Epidural

Psychiatric patients

Bleeding diathesis

H/o. hypersensitivity to Opioid /LA

In the preanaesthetic visit, all the patients were made familiar with the study plan. Respiratory rate, Non invasive blood pressure, peripheral arterial saturation and heart rate were monitored throughout the

perioperative period. Patients were monitored with pulse oximetry, NIBP & ECG. Respiratory rate also was recorded.

Intravenous Hydration with 12-15ml/kg of fluid prior to surgery. Epidural Catheter is placed in L2-L3 or L3-L4 interspace. Approximately 4cm of catheter was kept inside the space. A test dose of 2ml of 0.5% Bupivacaine was given via catheter before it is fixed. After confirming the epidural placement of the catheter, incremental doses of 0.5% Bupivacaine(5cc) was given until a bilateral T6 sensoroy level (determined by pin prick) was attained. Till the incision time parturient was placed in operating table in a left lateral tilt. Oxygen at 4L/min via venturi mask was provided. If there was any hypotension (MAP < 60 mm Hg) Inj. Ephedrine 6mg iv was given along with intravenous fluid. If the Heart rate fell below 50/mt, Inj Atropine 0.6mg iv was given.

Epidural route was used for surgery & postoperative analgesia. If the epidural block failed, regional anaesthesia was converted to General Anaesthesia and the parturient was excluded from the study. Opioid was not administered during the intraoperative period. After the surgery was over parturients were shifted to labour ward postoperative recovery room.

The parturients were observed for pain on a 10cm VAS. When the epidural effect of local anaesthetic given in the intraoperative period was wearing off & when they complained of pain (VAS of 5cm), they were

classed into four groups randomly as follows & study drugs were given epidurally for the respective groups.

Group 1 (NS): 20 parturients receiving 10ml of 0.125% Bupivacaine + 1ml of Normal Saline (Total = 11ml)

Group 2 (FENT): 20 parturients receiving 10ml of 0.125% Bupivacaine + 50ug of Fentanyl (1ml) (Total = 11ml)

Group 3 (NALB): 20 parturients receiving 10ml of 0.125% Bupivacaine + 5mg of Nalbuphine(0.5ml) +0.5ml of Normal saline to make it into 1ml (Total = 11ml)

Group 4 (BUTOR): 20 parturients receiving 10ml of 0.125% Bupivacaine + 1mg of Butorphanol (1ml) (Total = 11ml)

Pain score was observed at 2min, 4min, 6min, 8min, 10 min, 15 min, 20 min, 25 min, 30min & then every ½ hourly intervals upto 10hrs on a 10cm VAS (‘no pain’ at 0 cm end and ‘worst pain ever’ at 10cm end). The observer assessing pain was kept blinded for the epidural medication. Thereafter, continuous measurement of pain by VAS was made at intervals till the patient was completely free of pain (VAS 0). If the VAS score failed to decline atleast by 1cm even after 30 min of epidural injection, the patient was given intramuscular diclofenac sodium 75 mg and was excluded from the study.

The onset of analgesia was defined as the time from injection of the study medication to first reduction in pain intensity by at least 1cm in VAS; the onset of peak analgesia was defined as the time to achieve the lowest VAS score; and the duration of analgesia was defined as the time between the onset of analgesia and either a return to baseline VAS of 5cm (after which patients were given i.m diclofenac & study concluded). If any patient demanded pain relief before the study could be completed they were also given i.m diclofenac & were excluded from the study. The quality of analgesia was assessed based on the overall satisfaction of the patient and the time of the first changing of positions side to side independently in the bed. The overall satisfaction of the patient was assessed with a 10 cm scale of VAS Satisfaction ('no satisfaction' at 0 cm end and 'the best satisfaction' at 10 cm end). Motor block if any was assessed using the Bromage Score.

Sedation was assessed when the VAS score reached the minimum (using Modified Ramsay sedation score). The occurrence of nausea and vomiting, pruritus and respiratory depression (respiratory rate <10/min) was noted up to 24 hours following administration of the study medication.

The collected data was analyzed statistically: Analysis of variances (ANOVA) was used for comparison of mean values between more than two groups; Posthoc test was used to find any significance between the

individual groups, Chi square test was used to compare the discrete variables between groups. A p value of <0.05 was considered significant.

SCALES & SCORES USED

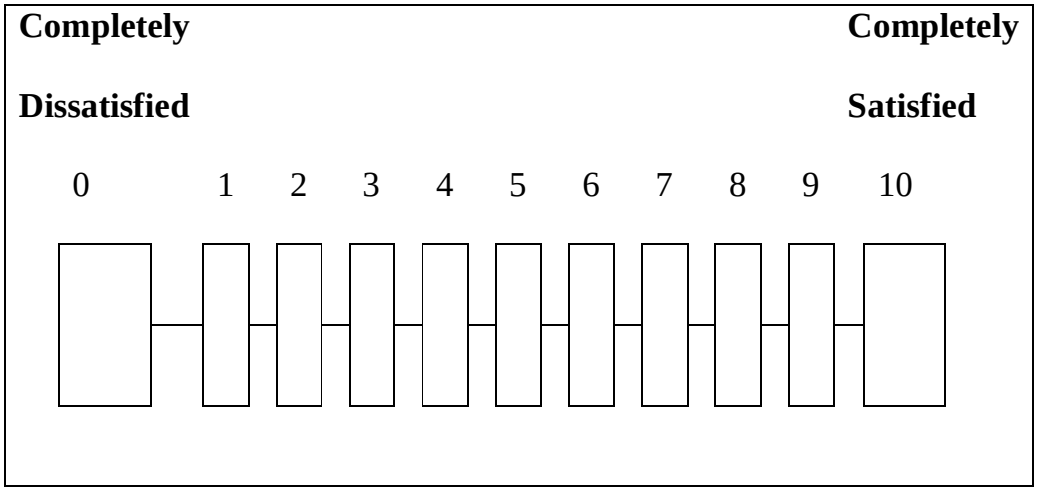
VISUAL ANALOGUE SCALE

"Please make a mark on this line that describes how much pain you are having"

No 0___1___2___3___4___5___6___7___8___9___10 **Worst**

pain **imaginable pain**

PATIENT SATISFACTION SCALE:



BROMAGE SCALE:

Grade	Criteria	Degree of block
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees, but with free movement of feet	Almost complete (66%)
IV	Unable to move legs or feet	Complete (100%)

Modified Ramsey Sedation Scale

1. anxious and agitated or restless, or both
2. co-operative, oriented, and calm
3. responsive to commands only
4. exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. exhibiting a sluggish response to light glabellar tap or loud auditory stimulus
6. unresponsive

Nausea / vomiting

0- No nausea/vomiting

1- Nausea

2- Vomiting

0 - No pruritus

1- Pruritus

Independent change of position

Patient able to change position side to side freely - 1

Not able to change position because of pain/discomfort – 0

Bradycardia HR < 50/min

0 - No Bradycardia

1- Presence of Bradycardia

Respiratory depression

RR < 10/mt

0 - No Respiratory depression

1 - Presence of Respiratory depression

Desaturation: SPO2 < 95%

0 - No desaturation

1 - Presence of desaturation

Hypotension

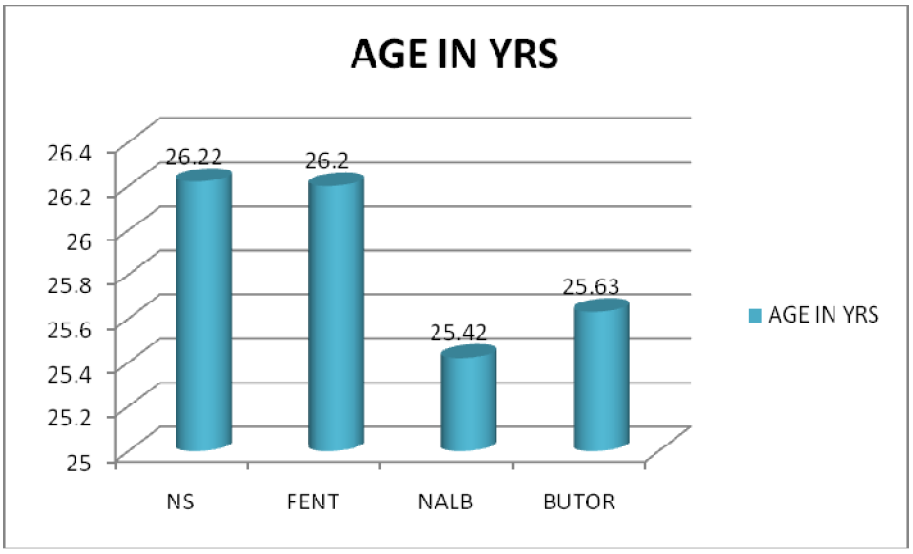
Systolic BP < 80 mm Hg

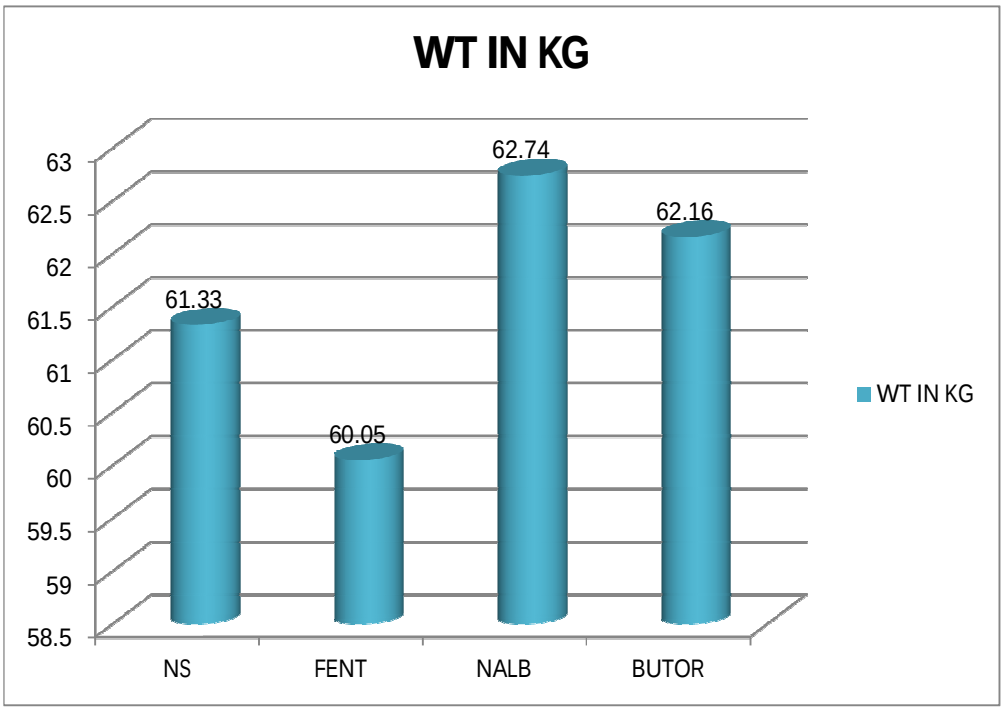
MAP < 60 mm Hg

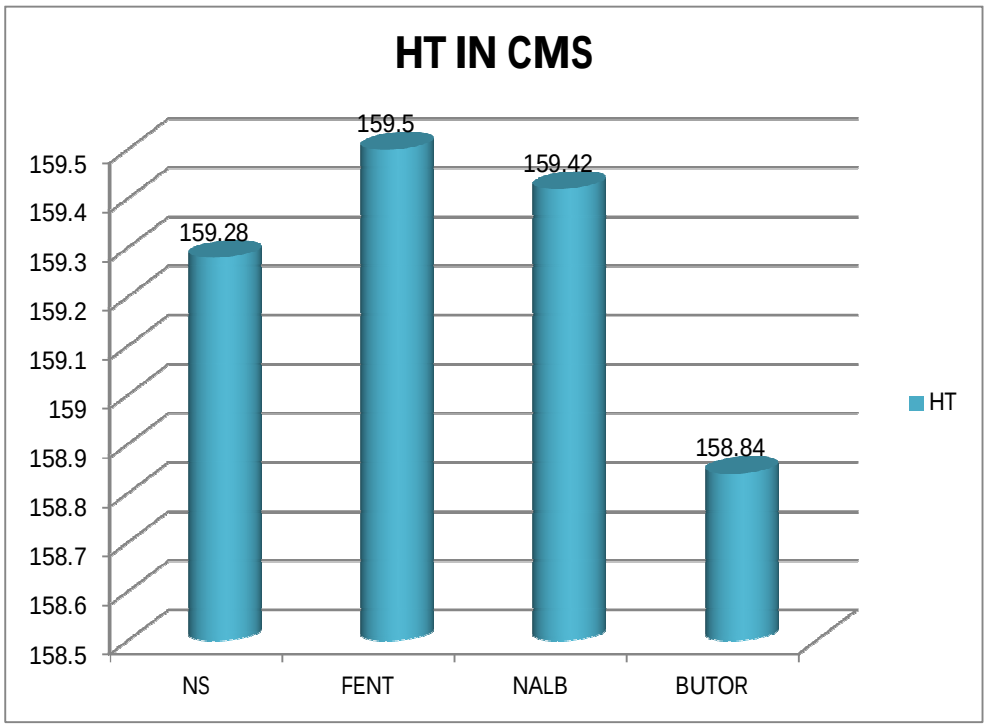
RESULTS

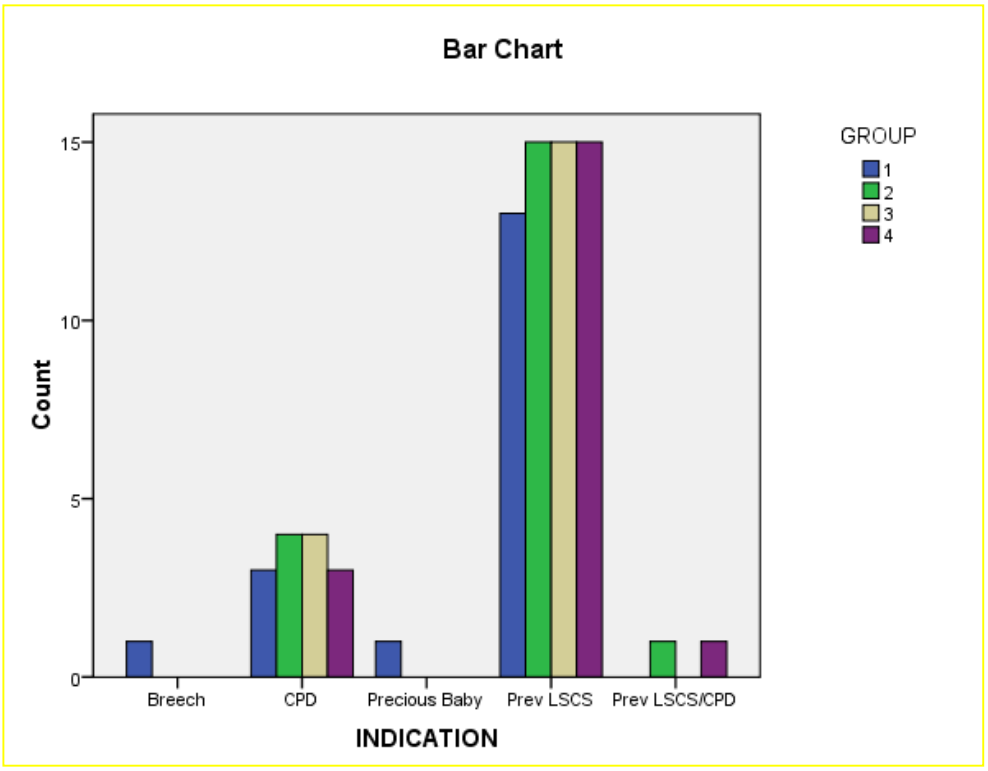
The data of only 77 patients were included for calculation because three patients were dropped from the study as they had patchy sensory blockade to an extent of converting to GA.There was no statistically significant difference in demographic parameters (age, height, weight); Indication for epidural; Epidural insertion space, volume of local anaesthetic given(0.5% Bupivacaine) (p value- 0.578) & duration of surgery (p value – 0.654) in the four groups.

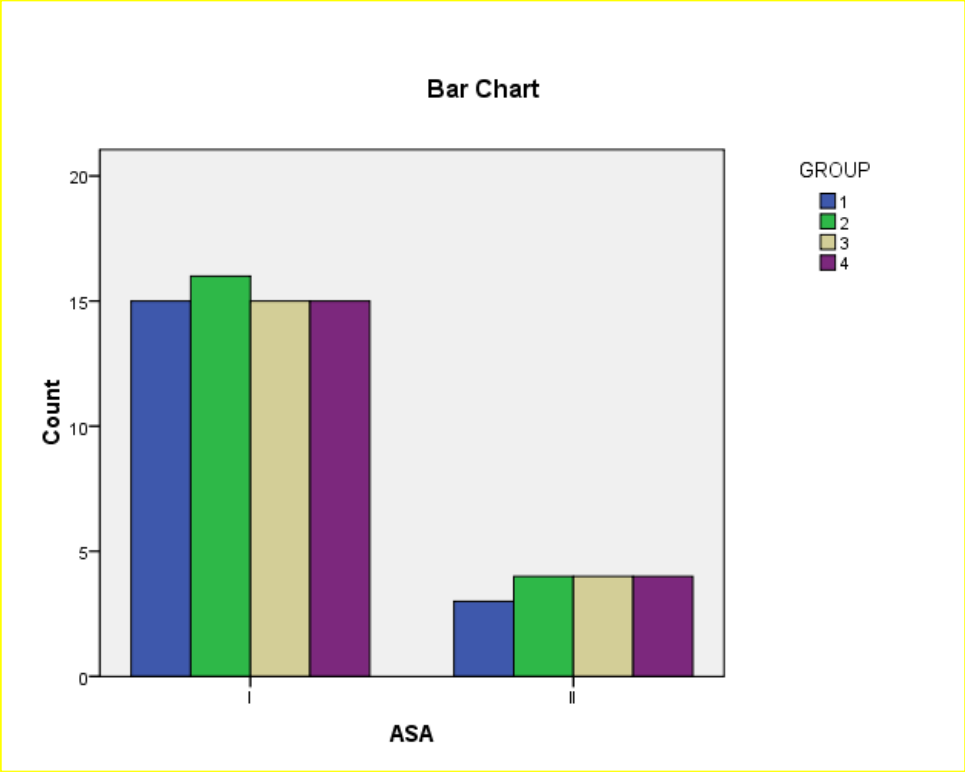
Serial No.	Parameter	Group NS (n=18)	Group FENT (n=20)	Group NALB (n=19)	Group BUTOR (n=19)	P value
1	Age (yrs)	26.22	26.20	25.42	25.63	0.766
2	Weight(kg)	61.33	60.05	62.74	62.16	0.707
3	Height(cm)	159.28	159.50	159.42	158.84	0.985


AGE IN YRS
26.4
26.2
26
25.8
25.6
25.4
25.2
25
26.22
26.2
25.42
25.63
NS
FENT
NALB
BUTOR
AGE IN YRS


WT IN KG
63
62.5
62
61.5
61
60.5
60
59.5
59
58.5
61.33
60.05
62.74
62.16
NS
FENT
NALB
BUTOR
WT IN KG


HT IN CMS
159.5
159.4
159.3
159.2
159.1
159
158.9
158.8
158.7
158.6
158.5
159.28
159.5
159.42
158.84
NS
FENT
NALB
BUTOR
HT

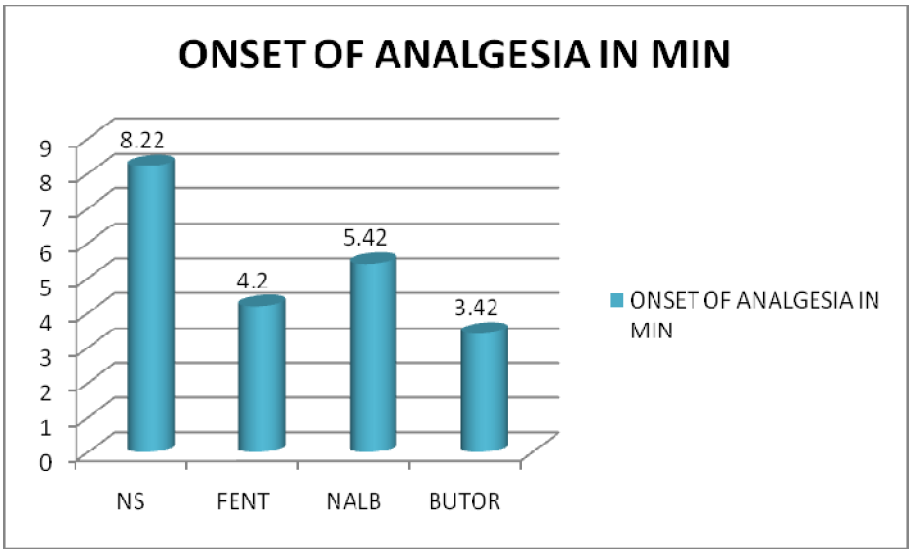

Bar Chart
15
10
5
0
Count
Breech
CPD
Precious Baby
Prev LSCS
Prev LSCS/CPD
INDICATION
GROUP
1
2
3
4

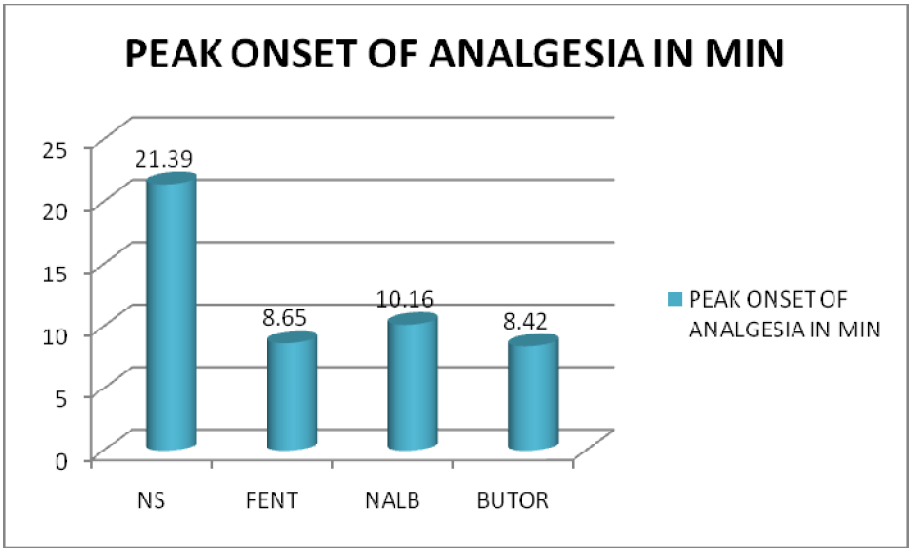


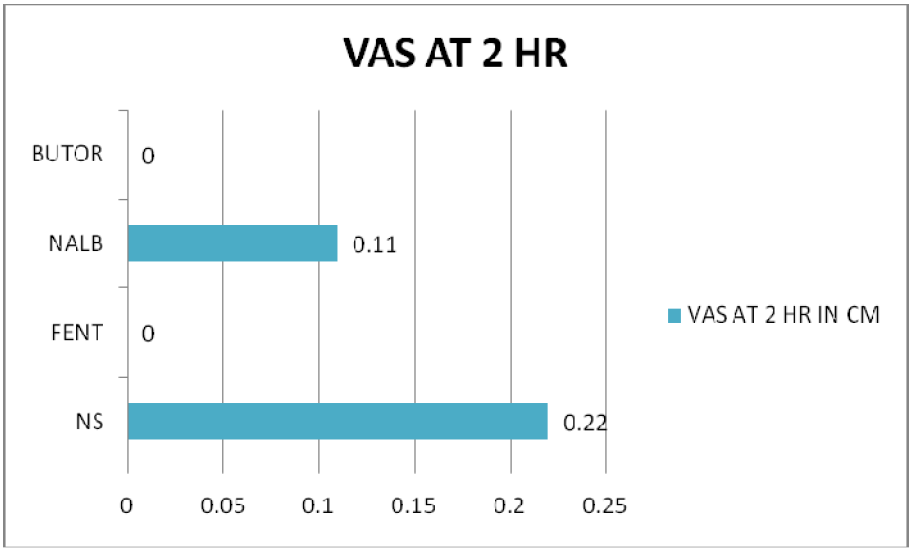
Mean onsets of analgesia and times to reach peak analgesia were significantly shorter while the mean durations of analgesia were significantly longer in the groups receiving fentanyl, nalbuphine & butorphanol than in the group receiving bupivacaine alone. Also there is a statistical significance between individual groups. The onset of analgesia was earliest with Butorphanol group followed by fentanyl group, Nalbuphine group & finally by control group. The onset of peak analgesia occurred first in the Butorphanol group followed by fentanyl group, Nalbuphine group & finally by control group. The duration of analgesia was maximum with Butorphanol group (mean of 360 min

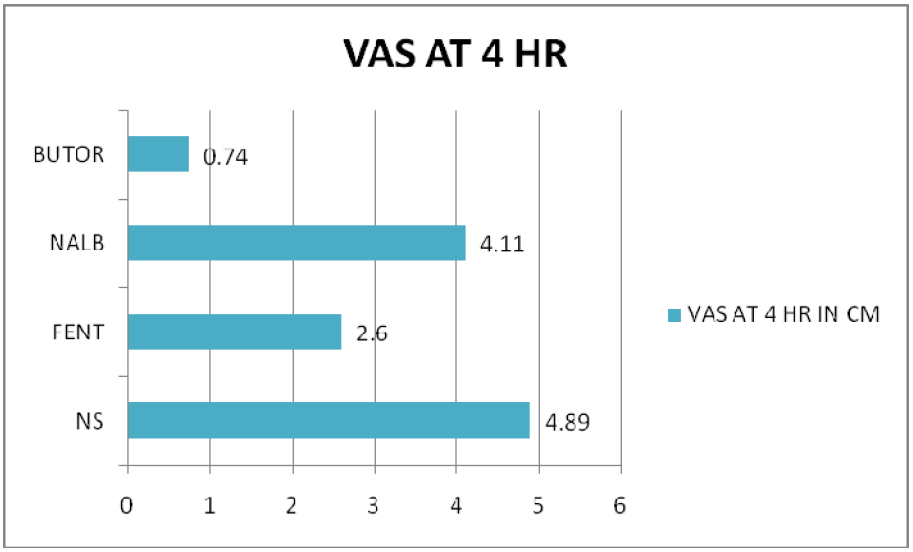
approx), followed by Fentanyl group (mean of 279 min approx), Nalbuphine group (mean of 246 min approx) & control group (mean of 212min approx).

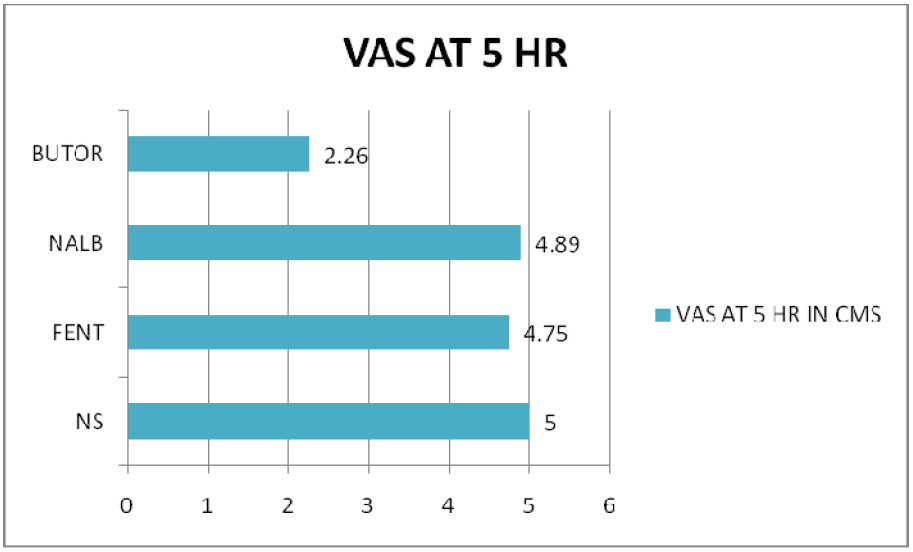
Sl. No.	Parameter (min)	Group NS (n=18)	Group FENT (n=20)	Group NALB (n=19)	Group BUTOR (n=19)	P value
1	Onset of analgesia	8.22	4.20	5.42	3.42	**0.000**
2	Peak onset of analgesia	21.39	8.65	10.16	8.42	**0.000**
3	Duration of analgesia	211.94	279.20	245.53	360.11	**0.000**

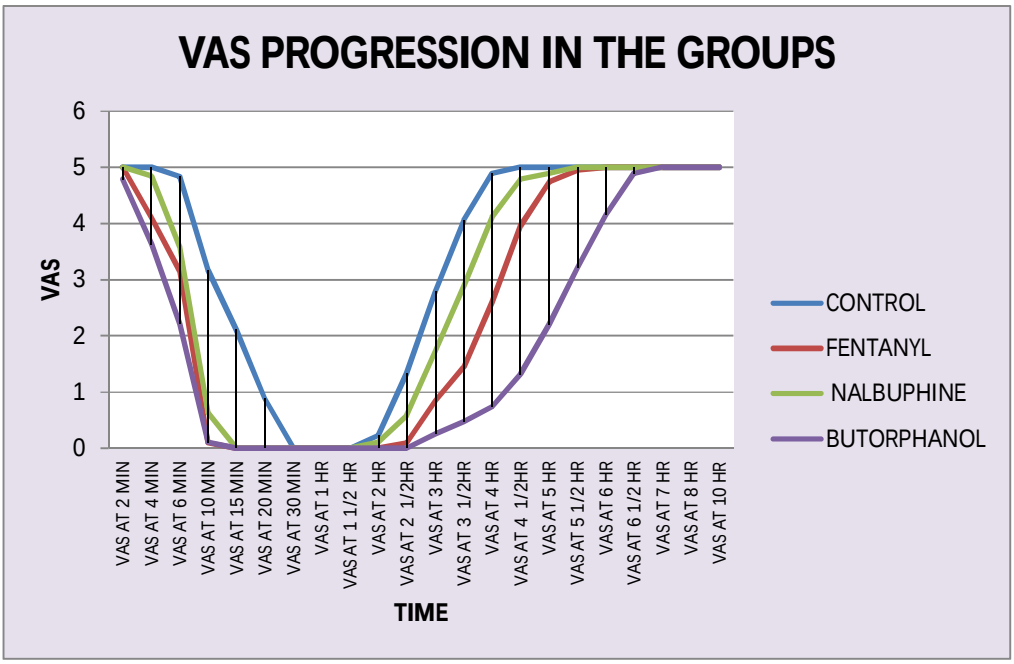


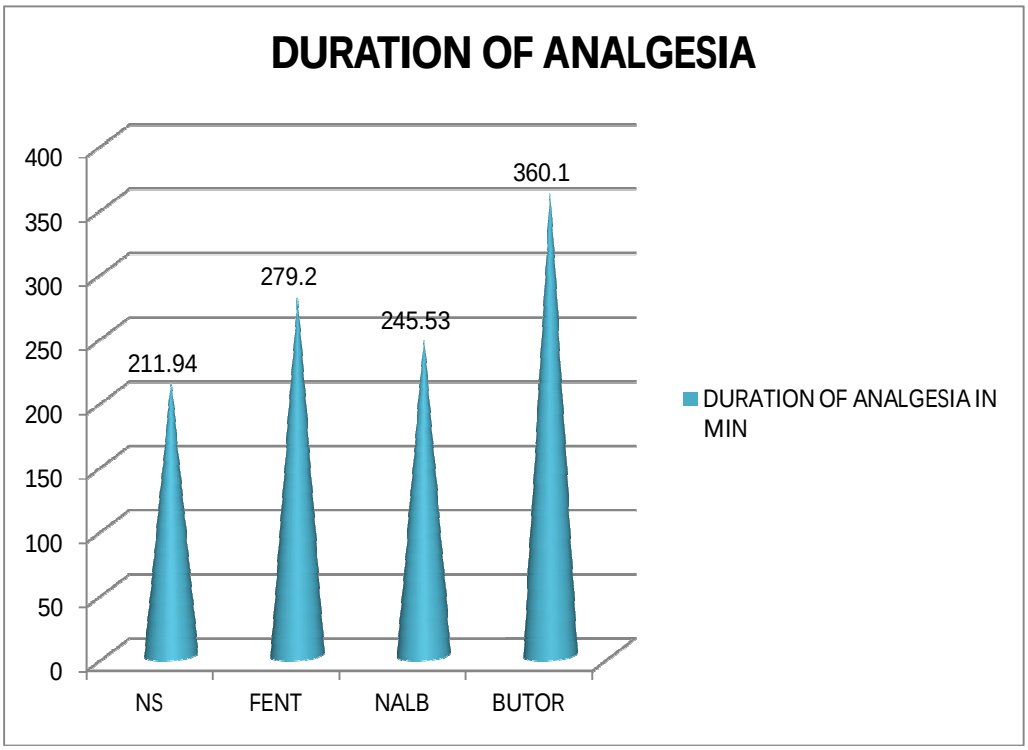

PEAK ONSET OF ANALGESIA IN MIN
25
20
15
10
5
0
21.39
8.65
10.16
8.42
NS
FENT
NALB
BUTOR
PEAK ONSET OF ANALGESIA IN MIN


VAS AT 2 HR
BUTOR
NALB
FENT
NS
0
0.11
0
0.22
0
0.05
0.1
0.15
0.2
0.25
VAS AT 2 HR IN CM


VAS AT 4 HR
BUTOR
NALB
FENT
NS
0.74
4.11
2.6
4.89
0
1
2
3
4
5
6
VAS AT 4 HR IN CM


VAS AT 5 HR
BUTOR
NALB
FENT
NS
2.26
4.89
4.75
5
0
1
2
3
4
5
6
VAS AT 5 HR IN CMS


VAS PROGRESSION IN THE GROUPS
VAS
TIME
0
1
2
3
4
5
6
VAS AT 2 MIN
VAS AT 4 MIN
VAS AT 6 MIN
VAS AT 10 MIN
VAS AT 15 MIN
VAS AT 20 MIN
VAS AT 30 MIN
VAS AT 1 HR
VAS AT 1 1/2 HR
VAS AT 2 HR
VAS AT 2 1/2HR
VAS AT 3 HR
VAS AT 3 1/2HR
VAS AT 4 HR
VAS AT 4 1/2HR
VAS AT 5 HR
VAS AT 5 1/2 HR
VAS AT 6 HR
VAS AT 6 1/2 HR
VAS AT 7 HR
VAS AT 8 HR
VAS AT 10 HR
CONTROL
FENTANYL
NALBUPHINE
BUTORPHANOL


DURATION OF ANALGESIA
0
50
100
150
200
250
300
350
400
211.94
279.2
245.53
360.1
NS
FENT
NALB
BUTOR
DURATION OF ANALGESIA IN MIN

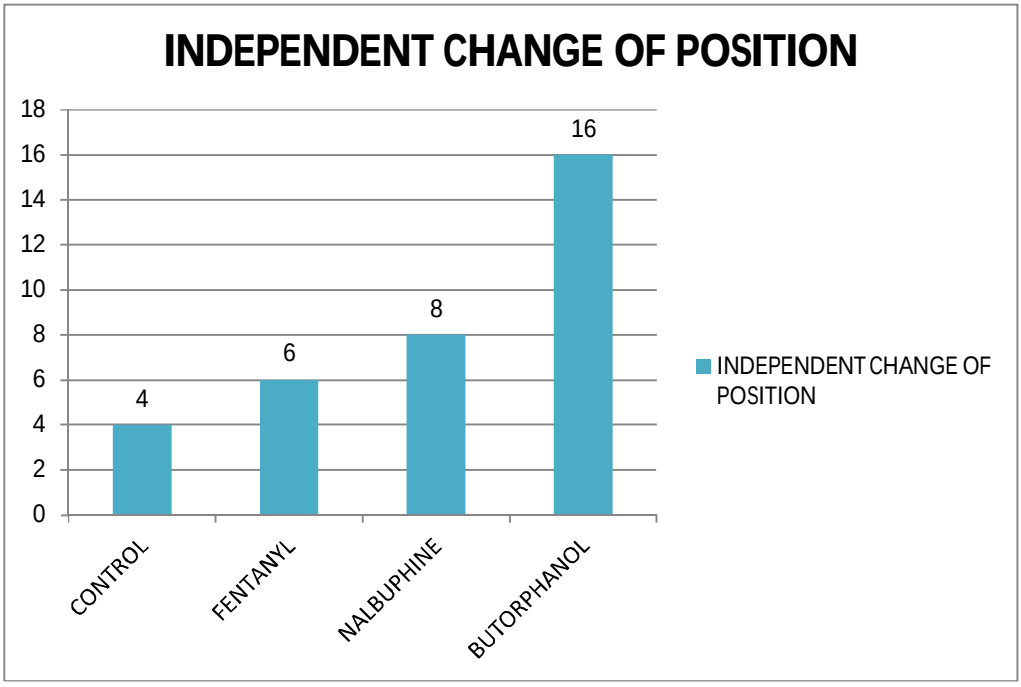
Satisfaction with the pain relief given was assessed by

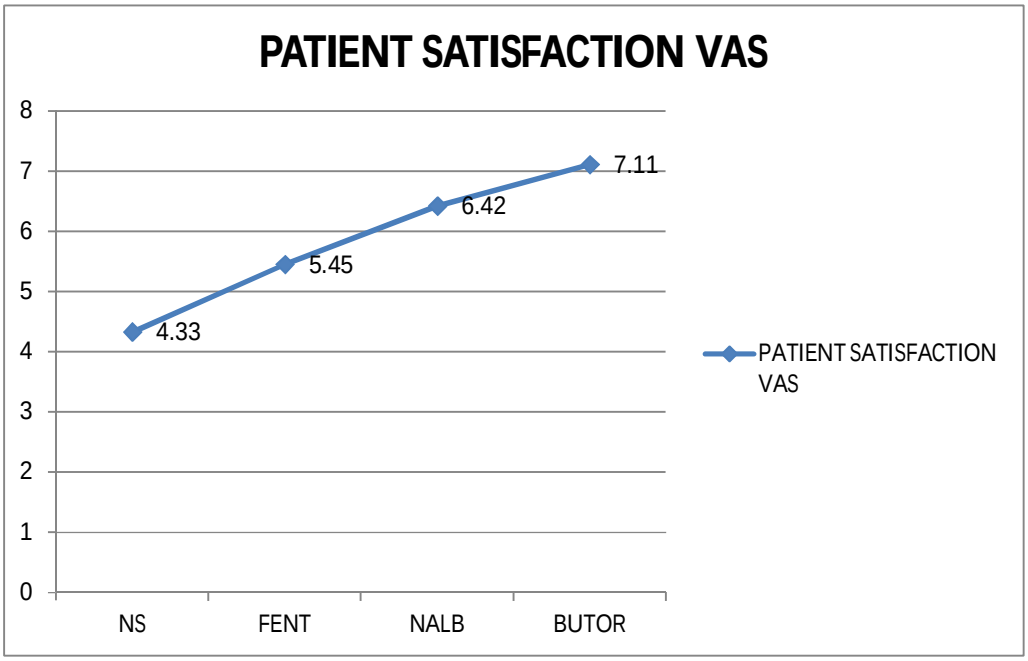
1. Ability for independent side to side movement

2. VAS for satisfaction.

It was observed that, mothers of Butorphanol group was able to turn side to side for feeding their babies, instead of the surgical trauma, better than nalbuphine group, fentanyl group & control group in the descending order. It was also observed that satisfaction was more with Butorphanol group followed by Nalbuphine group, Fentanyl group & by control group in the descending order.

Sl. No.	**Parameter (min)**	**Group NS (n=18)**	**Group FENT (n=20)**	**Group NALB (n=19)**	**Group BUTOR (n=19)**	**P value**
1	Independent Change of position	22%	30%	42%	84%	**0.001**
2	VAS for Satisfaction	4.33	5.45	6.42	7.11	**0.000**

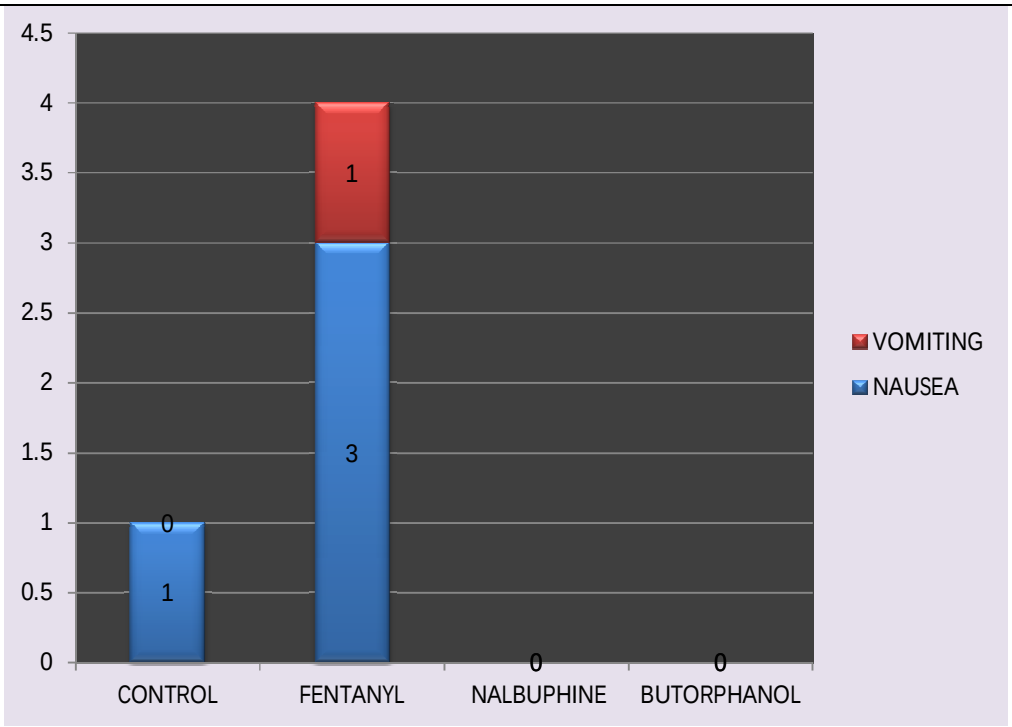




There were no motor blockade observed in any of the study groups (Bromage score was Grade I).

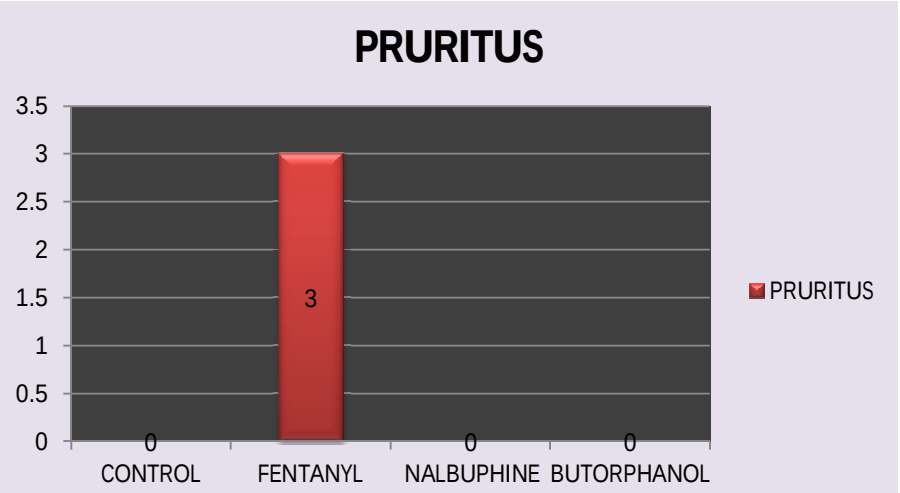
Nausea & Vomiting was observed in both control group (incidence of 6%) & fentanyl group (incidence of 20%)

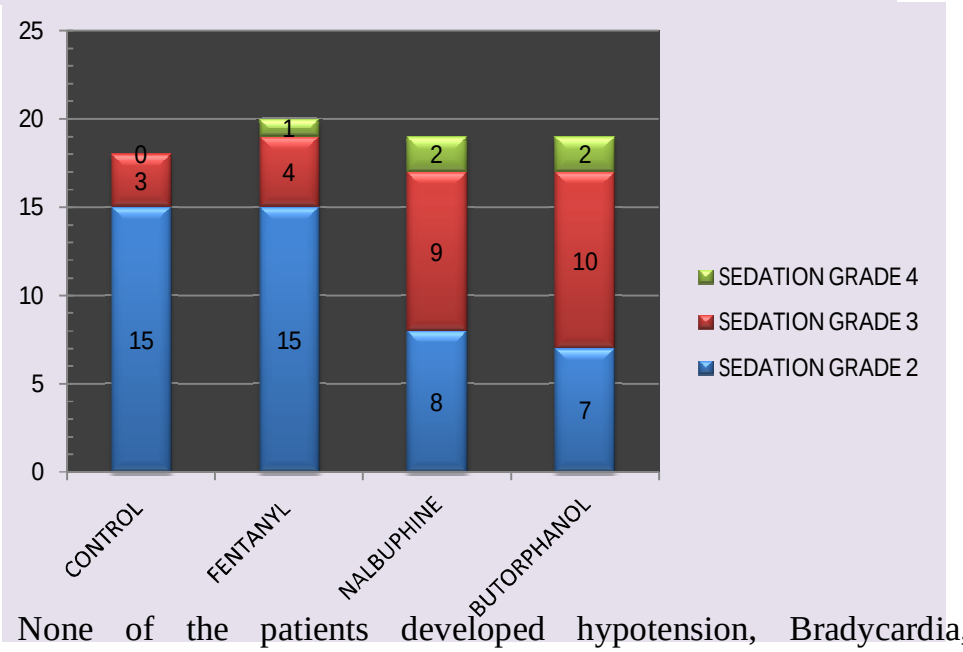
Sl No.	Parameter – Incidence	Group NS (n=18)	Group FENT (n=20)	Group NALB (n=19)	Group BUTOR (n=19)	P value
1	Nausea-vomiting	5.55 %	20 %	-	-	**0.000**
2	Pruritus	-	15 %	-	-	**0.033**
3	Sedation	16.66 %	25 %	57.89 %	63.16%	**0.000**
No patient in any of the group had Respiratory depression, Bradycardia, Hypotension, Desaturation						



Pruritus was observed only in the fentanyl group with a incidence of 15% .

Sedation was observed in all the groups (Control – 17%, Fentanyl – 25%, Nalbuphine – 58%, Butorphanol – 63%. Butorphanol & Nalbuphine groups had more incidence of sedation & higher grades of sedation (Grade 4).





None of the patients developed hypotension, Bradycardia, respiratory depression.

DISCUSSION

The analgesic efficacy & side effects of Epidural 0.125% Bupivacaine + Normal saline; 0.125% Bupivacaine + fentanyl 50ug; 0.125% Bupivacaine + Nalbuphine 5mg & 0.125% Bupivacaine + Butorphanol 1mg were studied.

1. The onset of analgesia was earlier & the duration of analgesia was prolonged in all the opioid groups when compared to the control group. The study has once again confirmed that combination of an opioid and a local anesthetic enhances the onset and prolongs the duration of analgesia more than the local anesthetic alone.

Results of our study correlate with study done by Abboud and coworkers who found significantly better quality of analgesia in parturients receiving epidural bupivacaine with butorphanol than with bupivacaine alone[29], *(epidural LA with opioid better than LA alone)*

Shrestha et al, in his study has shown that 2 mg of epidural butorphanol added to a lower concentration of bupivacaine (0.1%) provided a better quality of labor analgesia than 0.25% bupivacaine alone.[30] *(epidural LA with opioid better than LA alone)* which again correlate with our study.

2. Butorphanol in addition to bupivacaine produce earlier onset and longer duration of analgesia than Nalbuphine & Fentanyl in epidural analgesia. Epidural Butorphanol with bupivacaine also had better patient

satisfaction in terms of VAS for Satisfaction and ability for independent movement (position change).

Pokharel K et al in his study, Low dose (0.5 mg) of epidural butorphanol with bupivacaine 0.125% was studied in parturients following cesarean delivery. Parturients were allocated into two groups: group 1 received epidural 0.125% bupivacaine while group 2 received an additional of 0.5 mg butorphanol[(31)]. The epidural route was used for postoperative analgesia with the study drug. The onset and duration of analgesia in group 2 (4.1+/-2.6 min and 202.4+/-62.8 min) were significantly different (P<0.01) from group 1 (6.6+/-2.7 min and 145.7+/-89.6 min). Results we obtained were (Butorphanol group - onset of analgesia was 3.42 min, duration of analgesia was 360 min & NS group - onset of analgesia was 8.22 min, duration of analgesia was 211 min). Both the results are comparable, except for an early onset of analgesia & prolonged duration of analgesia we obtained in our study, which could probably attributed to a little higher dose (1mg of butorphanol) used in our study.

Gupta R et al in his study on Post operative analgesia in patients undergoing lower limb surgery with 2 mg butorphanol as bolus epidurally diluted in 10 ml normal saline, found the duration of analgesia to be 5.35±0.29 hrs. The duration of analgesia in this study was comparable to our study (duration = 360min).[(32)]

3. Nalbuphine in combination with bupivacaine produced delay onset & shorter duration of analgesia when compared to Fentanyl & Butorphanol groups, but definitely earlier onset and longer duration of analgesia than bupivacaine alone.

Though the onset of analgesia was delayed and duration of analgesia was short in the Nalbuphine group when compared to the fentanyl group, patient satisfaction was better in the Nalbuphine group, probably because the side effects like nausea/vomiting; pruritus are less with Nalbuphine compared to Fentanyl.

Baxter AD et al in his study, demonstrated that after cesarean delivery with epidural lidocaine, epidural Nalbuphine in doses of 10,20, and 30 mg promoted satisfactory analgesia, but with a duration of only 1-3 h[33]

Pugh GC et al[34], in his study mentioned nalbuphine as an analgesic agent provides a number of advantages. Used as the sole opioid analgesic, it can satisfactorily cover mild to moderate pain with a low incidence of side effects. The ceiling effect of nalbuphine, which prevents it from supplying sufficient analgesia to cover the most severe discomfort, also prevents increasing sedation and respiratory depression as the dose is increased, potentially providing an increased safety margin in comparison to mu-agonists. When nalbuphine is used concurrently with mu-agonists (e.g. morphine, fentanyl) the benefits of both mu- and

kappa-analgesia can be obtained, with simultaneously decreased incidence and severity of the common mu-agonist side effects (pruritis, nausea/emesis, constipation, urinary retention, respiratory depression and undesirable sedation).

4. Though the incidence of sedation is more in Butorphanol & Nalbuphine groups, all the patients were easily arousable. butorphanol is associated with profound dose-dependent sedation with reported somnolence in more than 50% of patients at doses 2 mg or more.[35]

In our study we have used only 1mg epidurally, hence the sedation cannot be fully attributed to the drug. The contribution of factors such as sleep deprivation, exhaustion and anxiety during surgery renders the patients drowsy or sleepy cannot be denied

5. In the study, we did not observe nausea and vomiting in Butorphanol & Nalbuphine groups. Fentanyl group had nausea & vomiting upto 20% more than control group(5.55%)

Cohen et al in his study for postcesarean analgesia, found epidural bupivacaine when combined fentanyl had more more nausea and vomiting than bupivacaine alone[36] which correlates with our study.

6. In the study, we did not observe pruritus in Butorphanol & Nalbuphine groups which could be compared with the following studies;

J S Naulty et al in his study on epidural Butorphanol after delivery of baby 1mg, 2mg, 4mg in 40 parturients, results showed increasing duration of analgesia as dose increases, but no statistical significance. No case reported pruritus. somnolence.

Prophylactic administration of butorphanol has been recommended for prevention of such side effects produced by pure agonist opioids like morphine and it has also been effectively used for the treatment of intractable pruritis associated with dermatological conditions[37]

Wittles et al found that epidural nalbuphine 10 mg reduced the incidence of pruritus from 48% to 20% for 6 h[38]

CONCLUSION

Epidural 0.125% Bupivacaine combined with Butorphanol produces significantly earlier onset, longer duration and better quality of analgesia than 0.125% Bupivacaine - Nalbuphine combination / 0.125% Bupivacaine -Fentanyl combination / 0.125% Bupivacaine alone and is safe in parturients.

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ETHICAL COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE, KILPAUK, CHENNAI- 10.

Venue: PANAGAL HALL, KMC

Dt: 01.06.2010

CHAIRPERSON

Prof. Dr.V.KANAGASABAI, MD.,

Dean

Govt. Kilpauk Medical College, Chennai-10

Sub: Ethical Committee project work - approved – regarding.

Ref: Lr.No.975/Audit/08 Dt. 01.06.2010.

With above reference, the Institutional Ethical committee meeting for the following students was conducted at out Institution on 01.06.2010.

Name	Topic
Dr.D.Jayakumar, III year Mch., (Surgical Oncology) PG	Usefulness of Image guided Biopsy in cancer Patients
Dr.P.Saravanan, III year Mch (Surgical Oncology) PG	Study in Government Royapettah Hospital regarding the experience with aggressive Fibromatosis from 1996 to Till date
Dr.C.Amutha, I year MD Micro Biology	Bacterial Profile of Neonatal Sepsis
Dr.J.Meharunnissa, I year MD Microbiology	Bacteriological profile in burns unit and their antibiotic susceptibility pattern at EMCH, Chennai
Dr.P.Venkateswaran, M.S.ENT	Anatomical Variations of the osteomeatal complex as a cause of chronic sinusitis and its correlation with the surgical result following functional endoscopic sinus surgery.
Dr.A.Arumagiri, MCh (Urology) PG	Comparative study of efficacy of localization and Fragmentation of renal stone by USG and Fluroscopy Guided ESWL.
Dr.J.Sivabalan, Mch Urology	Outcome of tension free trans obturator tape for female stress urinary incontinence.

Dr.N.Dinesh Kumar, PG Paediatrics	To asses the role of parenteral steroids on the clinical course and outcome of Meconium Aspiration Syndrome in newborn.
Dr.A.Karthik, PG Anaesthesiology	Comparison of Epidural Opioid-LA combination for Post Cesarean Analgesia
Dr.J.Rajaram, PG Anaesthesiology	Synergistic effect between dexmedetomidine and 0.75% Ropivacaine in Epidural.
Dr.K.Venkatesan, PG Anaesthesiology	Magnesium sulphate as an adjuvant to Intrathecal Bupivacaine in patients with mild preeclampsia undergoing caesarean section – Depth of Anaesthesia.

We are glad to inform you that at the Ethical Committee meeting the documents were discussed and the above short term projects are Ethically approved.

CHAIRPERSON 7/6/10

Prof. Dr.V.KANAGASABAI, MD.,
Dean
Govt. Kilpauk Medical College,
Chennai-10.

To
The Individuals

PROFORMA

NAME: AGE: GRAVIDA:

OCCUPATION: ADDRESS: WEIGHT:

ANAESTHETIST:

PREOPERATIVE CLINICAL ASSESMENT:

H/O MEDICAL / SURGICAL ILLNESS:

PALLOR/CLUBBING/PEDAL EDEMA/CYANOSIS:

CVS: VITALS: PR-

RS: BP-

OTHER SYSTEMS:

INVESTIGATIONS:

BLOOD HB%: RFT: BLOOD SUGAR:

ECG:

AIRWAY:

ASA PHYSICAL STATUS:

PREOPERATIVE CLINICAL ASSESMENT ON THE DAY OF SURGERY:

PROFORMA FOR STUDY GROUP _____

S.NO	Variable	Data	VAS	
	Anaesthetist		2 min	
1.	Name		4 min	
2.	Age		6min	
3.	IP No.		8 min	
4.	Gravida		10 min	
5.	Indication		15 min	
7.	Comorbid Illness		20 min	
8.	Height		25 min	
9.	Weight		30 min	
10.	ASA		1 hr	
11	Epidural space		1 ½ hr	
12	Catheter length inside space		2 hr	
13.	Vol. of 0.5% sensorcaine		2 ½ hr	
14.	Highest level achieved		3 hr	
15.	Incision Time		3 ½ hr	
16.	Time of baby delivery		4 hr	
17.	Time at which surgery was finished		4 ½ hr	
18.	Duration of Surgery		5 hr	
19.	Time at which pain (VAS = 5) in postoperative period		5 ½ hr	
20.	Duration of motor block		6 hr	
21.	Motor blockade grade		6 ½ hr	
22.	Duration of Analgesia		7 hr	
23.	Nausea/Vomiting		8 hr	
24.	Pruritus		9 hr	
25.	Sedation grade		10 hr	
26.	Respiratory depression		Onset of analgesia duration	
27.	Hypotension		Peak onset of analgesia	
28.	Bradycardia		Duration of analgesia	
29.	Desaturation		Independent change of position	
			VAS for satisfaction	

MASTER CHART: FOUR GROUPS

S.NO.	NAME	AGE	HT(cm)	SPACE	CATH	VOLUME	VED	DUR	LEVEL	POSTOP (VAS SCORES)	VAS	VAS	VAS	VAS	VAS	A VAS	A VAS	A VAS	A VAS	A VAS	AT VAS	AT VAS	AT VAS	AT VAS	AT VAS	AT VAS	AT VAS	AT VAS	AT VAS	ONSET	PEAK	ANAL	DURATION	O2 PATIENT SA	INDEPENDED	BRO	MAGE	BRADYC	HYPOT	DESAT	NAUSEA	SEDA	PRUI	RESPIRATORY	DEPRE
											2min	4min	6min	8min	10min	15min	20min	25min	30min	1h	1 1/2hr	2hr	2 1/2hr	3hr	3 1/2hr	4hr	4 1/2hr	5hr	5 1/2hr	6hr	6 1/2hr	7hr	8hr	10hr														
GROUP A		Drug injected - 10 ml of 0.125% Sensorcaine with 1 ml of NORMAL SALINE																																												
1	Devaki	28	163	2-L3	4	13	T5	53	T6	81	11.24 AM	5	5	5	4	3	3	2	0	0	0	0	0	0	2	3	5							8	25	222	4	0	Grade I	0	0	0	0	2	0	0
2	Renuka	26	155	3-L4	4.5	13	T4	42	T6	70	11.00 AM	5	5	4	3	3	2	0	0	0	0	0	0	0	1	2	4	5						6	20	252	5	1	Grade I	0	0	0	0	2	0	0
3	Gomathy	25	152	3-L4	4	12	T6	49	T7	68	12.10 PM	5	5	5	3	3	2	0	0	0	0	0	0	1	2	4	5							8	20	215	5	0	Grade I	0	0	0	0	3	0	0
4	Mary	28	156	3-L4	4.5	13	T5	55	T6	70	11.14 AM	5	5	5	5	4	3	2	0	0	0	0	0	1	2	3	5							10	25	230	4	0	Grade I	0	0	0	0	2	0	0
5	Kasthuri	28	155	2-L3	4.5	13	T4	40	T4	80	11.55 AM	5	5	5	4	3	2	2	0	0	0	0	1	2	3	5								8	25	205	4	0	Grade I	0	0	0	0	2	0	0
6	Surekha	26	161	3-L4	4	14	T4	62	T5	93	12.40 PM	5	5	5	4	3	2	0	0	0	0	0	0	2	4	5								8	20	194	4	0	Grade I	0	0	0	0	3	0	0
7	Shanthi	24	151	3-L4	4	13	T4	67	T5	109	1.00 PM	5	5	5	4	3	0	0	0	0	0	0	0	1	2	3	5							8	15	232	4	1	Grade I	0	0	0	0	2	0	0
8	Dhanalal	23	163	2-L3	4	13	T6	79	T8	78	12.12 PM	5	5	5	5	4	4	3	2	0	0	0	0	0	2	3	5							8	25	205	4	0	Grade I	0	0	0	0	2	0	0
9	Latha	23	153	3-L4	4	13	T4	60	T5	70	11.55 AM	5	5	5	5	4	3	2	0	0	0	0	0	0	1	2	3	5						8	20	235	3	0	Grade I	0	0	0	1	2	0	0
10	Saritha	28	170	2-L3	4	13	T5	50	T5	74	11.50 AM	5	5	5	5	5	4	3	2	0	0	0	0	0	1	2	3	4	5					10	25	244	5	1	Grade I	0	0	0	0	2	0	0
11	Dhatcha	26	160	3-L4	4	14	T5	53	T6	64	11.12 AM	5	5	5	5	4	3	2	0	0	0	0	1	2	3	5								8	20	178	4	0	Grade I	0	0	0	0	2	0	0
12	Lakshmi	25	163	2-L3	4	13	T5	46	T6	90	1.15 PM	5	5	5	4	3	2	0	1	1	1	1	0	1	2	3	5							6	15	205	4	0	Grade I	0	0	0	0	2	0	0
13	Kalaiselv	22	155	3-L4	4	14	T4	39	T4	100	1.45 PM	5	5	5	5	4	3	2	0	0	0	0	0	1	2	2	3	5						8	20	232	4	0	Grade I	0	0	0	0	2	0	0
14	Banumai	32	162	2-L3	4	13	T6	49	T6	84	1.05 PM	5	5	5	5	5	4	2	2	0	0	0	0	1	2	3	5							10	25	200	5	0	Grade I	0	0	0	0	2	0	0
15	Velankar	30	164	2-L3	4	12	T6	48	T6	75	12.40 PM	5	5	5	5	4	3	2	0	0	0	0	0	2	3	5								8	20	176	4	0	Grade I	0	0	0	0	2	0	0
16	Shalini	24	161	2-L3	4	13	T5	52	T6	76	12.05 PM	5	5	5	5	5	3	3	2	0	0	0	0	1	2	4	5							10	25	166	4	0	Grade I	0	0	0	0	2	0	0
17	Anitha	25	164	2-L3	4	14	T5	55	T5	86	12.38 PM	5	5	5	5	5	4	3	2	0	0	0	0	1	2	3	5							10	25	204	6	1	Grade I	0	0	0	0	3	0	0
18	Hajeena	26	159	2-L3	4	12	T5	47	T5	110	2.13 PM	5	5	4	3	2	0	0	0	0	0	0	0	1	2	2	4	5						6	15	200	5	0	Grade I	0	0	0	0	2	0	0
19	Akshaya	27	151	3-L4	4	12	Patient had no sensory blockade even after waiting for 15 , hence converted to spinal anaesthesia - dropped from study																																									
20	Vijaya	30	160	3-L4	4.5	13	T4	69	T5	82	1.00 PM	5	5	5	5	5	5	5	5	5	dropped out from study																										

S.NO.	NAME	AGE	HT(cm)	SPACE	CATH VOL	HEIGHT	DURA LEVEL	POSTOP (VAS SCORE 5)	VAS I	VAS I	VAS I	VAS A	VAS A	VAS A	VAS A	VAS A	VAS AT	VAS AT	VAS AT	VAS AT	VAS AT	VAS AT	VAS AT	VAS AT	VAS AT	VAS	VAS	ONSET	PEAK A	DURATI	PATIE	INDEF	BRDYPAGE	BRADYC	HYPOTO	DESAT	NAUSEA	SEDA	PRUI	RESPIRATORY	DEPRESSION
									2min	4min	6min	8min	10min	15min	20min	25min	30min	1h	1H2hr	2hr	2H2hr	3hr	3H2hr	4hr	4H2hr	5hr	5H2hr	6hr	6H2hr	7hr	8hr	10hr									
GPCUPB		Drug injected - 10 ml of 0.125% Sensorcaine with						50ug of	FENTANYL																																
1	Devi	26	152	3-L4	3.5	12	T5	51	T6	66	11.55 am	5	3	2	0	0	0	0	0	0	0	0	0	1	2	3	5			3	8	265	7	0	Grade I	0	0	0	0	2	0	0
2	Ponmani	27	170	2-L3	4	13	T4	53	T6	62	11.37 am	5	5	3	2	0	0	0	0	0	0	0	0	0	2	3	4	5		5	10	275	5	1	Grade I	0	0	0	1	3	0	0
3	Ilayarani	30	155	2-L3	4	13	T5	50	T6	78	1.00 pm	5	4	2	0	0	0	0	0	0	0	0	0	0	1	3	5			4	8	295	7	0	Grade I	0	0	0	0	2	0	0
4	Saraswa	23	158	2-L3	4	13	T6	75	T8	48	12.35 pm	5	4	2	0	0	0	0	0	0	0	0	0	1	2	3	5			4	8	285	6	0	Grade I	0	0	0	0	2	0	0
5	Eeswari	24	162	2-L3	4	13	T5	35	T5	92	1.30 pm	5	3	2	0	0	0	0	0	0	0	0	0	0	2	3	4	5		3	8	310	7	1	Grade I	0	0	0	0	2	0	0
6	Bharathi	29	158	3-L4	4	13	T6	48	T8	56	12.45 pm	5	5	4	2	0	0	0	0	0	0	0	0	0	0	2	3	4	5	6	10	338	6	1	Grade I	0	0	0	0	2	0	0
7	Vijayalak	24	150	3-L4	3.5	12	T5	55	T6	82	12.52 pm	5	4	2	0	0	0	0	0	0	0	0	0	0	1	2	3	5		4	8	315	6	0	Grade I	0	0	0	0	2	0	0
8	Maliga	23	154	3-L4	3.5	13	T4	82	T5	68	1.15 pm	5	4	3	2	0	0	0	0	0	0	0	0	0	2	5				4	10	260	7	0	Grade I	0	0	0	0	3	0	0
9	Bhuvane	29	161	2-L3	4	13	T5	39	T5	74	11.05 am	5	4	2	0	0	0	0	0	0	0	0	0	0	1	3	5			4	8	295	7	1	Grade I	0	0	0	0	4	0	0
10	Parvathi	32	158	2-L3	4	13	T4	35	T4	105	11.43 am	5	4	3	2	0	0	0	0	0	0	0	0	0	1	3	5			4	9	287	6	1	Grade I	0	0	0	0	2	0	0
11	Ramani	28	165	2-L3	4	14	T5	66	T7	45	12.05 pm	5	5	4	3	1	0	0	0	0	0	0	0	0	1	2	3	5		6	12	280	2	0	Grade I	0	0	0	2	2	1	0
12	Iswariya	26	163	2-L3	4	13	T6	41	T6	56	11.15 am	5	4	2	0	0	0	0	0	0	0	0	0	1	1	2	5			4	8	234	3	1	Grade I	0	0	0	1	3	0	0
13	Revathi	26	153	3-L4	4	13	T5	55	T6	62	11.35 am	5	3	2	0	0	0	0	0	0	0	0	0	0	1	2	3	5		3	7	258	4	0	Grade I	0	0	0	0	2	1	0
14	Lavanya	23	151	3-L4	3.5	12	T6	42	T6	45	11.54 am	5	4	4	2	0	0	0	0	0	0	0	0	0	1	2	2	5		4	10	265	5	0	Grade I	0	0	0	0	2	0	0
15	Jaya	22	152	3-L4	4	12	T6	50	T8	35	10.55 am	5	5	2	0	0	0	0	0	0	0	0	0	0	2	2	3	5		5	8	252	5	0	Grade I	0	0	0	0	2	0	0
16	Prema	30	167	2-L3	4	13	T5	45	T6	57	11.20 am	5	5	4	2	0	0	0	0	0	0	0	0	0	1	2	3	5		6	10	295	5	0	Grade I	0	0	0	0	2	0	0
17	Radhika	26	155	2-L3	4	13	T6	73	T7	45	11.45 am	5	3	1	0	0	0	0	0	0	0	0	0	0	1	2	3	5		3	8	265	6	0	Grade I	0	0	0	0	3	0	0
18	Abhilaksh	25	160	2-L3	4	13	T5	70	T6	75	11.35 am	5	4	2	0	0	0	0	0	0	0	0	0	0	1	2	3	5		4	7	260	4	0	Grade I	0	0	0	1	2	1	0
19	Mohana	25	172	2-L3	4	14	T4	43	T5	85	12.11 pm	5	4	2	0	0	0	0	0	0	0	0	0	0	2	3	5			4	8	270	6	0	Grade I	0	0	0	0	2	0	0
20	Kamatch	26	164	2-L3	4	13	T5	54	T6	65	12.30 pm	5	3	2	0	0	0	0	0	0	0	0	0	0	1	2	2	4	5	4	8	280	5	0	Grade I	0	0	0	0	2	0	0

S.NO.	NAME	AGE	HT(cm)	SPACE	CATH	VOLUMEINJED	DURA LEVEL	POSTOP (VAS SCORES)	VAS i	VAS ii	VAS iii	VAS iv	VAS A	VAS B	VAS A	VAS B	VAS A	VAS B	VAS i	VAS AT	VAS i	VAS AT	VAS i	VAS AT	VAS	VAS AT	VAS	VAS AT	VAS	VAS AT	VAS	VAS AT	VAS	VAS	VAS i	ONSE	PEAK A	DURATI	PATIE	NDEF	BRDYMAGE	BRADYC	HYPOTI	DESAT	NAUSEA	SEDA	PRUI	RESPIRATORY	DEPRESSION
									2min	4min	6min	8min	10min	15min	20min	25min	30min	1h	1HR2hr	2hr	2HR3hr	3hr	3HR3hr	4hr	4HR3hr	5hr	5HR3hr	6hr	6HR3hr	7hr	8hr	10hr																			
GROUP C		Drug injected - 10 ml of 0.125% Sensorcaine with 5mg of NALBUPHINE																																														
1	Vidhya	23	165	2-L3	4	13	T4	30	T4	116	11.45 am	5	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0	1	3	5				6	10	322	6	1	Grade I	0	0	0	0	3	0	0
2	Thamara	24	154	3-L4	4	12	T6	40	T6	65	2.10 PM	5	5	4	2	0	0	0	0	0	0	0	0	2	3	5								6	10	235	7	0	Grade I	0	0	0	0	4	0	0
3	Meena	27	153	3-L4	3.5	12	T6	54	T7	52	12.25 PM	5	5	3	3	1	0	0	0	0	0	0	1	1	2	3	5							5	11	265	6	0	Grade I	0	0	0	0	2	0	0
4	Parveen	23	160	2-L3	4	13	T5	55	T6	75	1.45 PM	5	4	3	2	0	0	0	0	0	0	0	0	2	3	4	5							4	9	250	6	1	Grade I	0	0	0	0	3	0	0
5	Lakshmi	33	158	2-L3	4	13	T5	58	T5	87	1.25 PM	5	5	4	3	2	0	0	0	0	0	0	0	2	4	5								6	12	218	5	0	Grade I	0	0	0	0	2	0	0
6	Lalitha	26	152	3-L4	4	12	T6	42	T6	72	12.35 PM	5	5	3	2	0	0	0	0	0	0	0	1	2	3	5								5	10	232	7	0	Grade I	0	0	0	0	4	0	0
7	Chithra	27	166	2-L3	4	13	T4	40	T4	105	1.00 PM	5	5	3	2	0	0	0	0	0	0	0	0	2	3	5								5	10	240	7	1	Grade I	0	0	0	0	3	0	0
8	Anju	27	155	3-L4	4	13	T4	36	T6	58	11.30 AM	5	5	4	3	2	0	0	0	0	0	0	0	2	3	5								6	11	236	6	0	Grade I	0	0	0	0	2	0	0
9	Deepa	24	165	2-L3	4	14	T5	55	T7	95	12.50 PM	5	5	3	2	1	0	0	0	0	0	0	2	4	5									5	11	178	5	0	Grade I	0	0	0	0	2	0	0
10	Dakshay	20	154	3-L4	4	12	T4	51	T5	84	12.43 PM	5	5	4	2	0	0	0	0	0	0	0	0	1	2	4	5							6	9	261	8	1	Grade I	0	0	0	0	3	0	0
11	Jhansi R	23	171	2-L3	4	14	T4	47	T6	90	1.13 PM	5	5	4	2	0	0	0	0	0	0	0	0	2	5									6	9	205	6	0	Grade I	0	0	0	0	2	0	0
12	Kalaivan	28	160	2-L3	4	13	T5	80	T7	68	11.45 AM	5	5	3	2	0	0	0	0	0	0	0	1	2	4	5								6	10	230	6	1	Grade I	0	0	0	0	3	0	0
13	Nithya	23	159	2-L3	4	13	T4	45	T5	87	12.00 PM	5	5	4	3	2	0	0	0	0	0	0	0	2	3	5								6	12	235	7	0	Grade I	0	0	0	0	3	0	0
14	Divya	20	152	3-L4	3.5	12	T6	34	T6	102	1.10 PM	5	5	4	2	0	0	0	0	0	0	0	0	1	2	4	5							6	9	252	7	0	Grade I	0	0	0	0	3	0	0
15	Rohini	27	165	2-L3	4	13	T4	78	T7	52	12.35 PM	5	5	3	2	0	0	0	0	0	0	0	0	0	2	3	5							5	9	265	8	0	Grade I	0	0	0	0	3	0	0
16	Jameela	25	160	2-L3	4	13	T6	40	T6	80	12.52 PM	5	4	3	1	0	0	0	0	0	0	0	0	1	3	5								4	10	240	6	1	Grade I	0	0	0	0	2	0	0
17	Gajalaks	30	159	2-L3	4	13	T5	48	T6	78	1.04 PM	5	4	3	2	2	0	0	0	0	0	0	0	0	1	3	5							4	13	260	6	1	Grade I	0	0	0	0	2	0	0
18	Narmadh	29	166	2-L3	4	13	T6	60	T8	58	12.55 PM	5	5	4	2	0	0	0	0	0	0	0	0	0	1	3	4	5						6	9	275	7	1	Grade I	0	0	0	0	3	0	0
19	Christopl	24	155	2-L3	4	12	T5	55	T7	70		5	5	4	2	0	0	0	0	0	0	0	0	0	2	3	5							6	9	266	6	0	Grade I	0	0	0	0	2	0	0
20	Banu	34	161	2-L3	4	13	Sensory Block was patchy, hence converted to GA																																									

S.N	NAME	AGE	HT (c	PACE	CAT	VOLVED	DURVEL	POST\ SCORE 5)	VA\	VA\	VA\	VA\	VAS	VAS	VAS	VAS	VA\	VA\	VAS	VA	VAS	VA	VAS	VA	VAS	VA	VAS	VA	VA\	VA\	ONK	PEAK	DURA	PAT	INDE	BROMA	BRAE	HYP	DES)	NAUS	SED	PRI	RESPIRATORY	DEPRESSION
GROUP D	Drug injected - 10 ml of 0.125% Sensorcaine with 1mg of BUTORPHANOL																																												
1	Jaya	24	160	pace	4	13	T5	43	T6	84	12:13 PM	5	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	3	4	5		3	8	383	8	1	Grade I	0	0	0	0	3	0	0
2	Rekha	24	161	pace	4	13	T6	50	T7	70	11:55 AM	4	3	2	0	0	0	0	0	0	0	0	0	0	0	0	1	2	3	4	5		2	8	345	7	1	Grade I	0	0	0	0	3	0	0
3	Shanthi	27	158	pace	4	13	T4	54	T5	100	1:05 PM	5	4	3	2	0	0	0	0	0	0	0	0	0	0	0	0	1	3	3	4	5		4	10	377	8	1	Grade I	0	0	0	0	3	0	0
4	Uma	30	160	pace	4	13	T5	51	T6	72	12:32	5	4	3	1	0	0	0	0	0	0	0	0	0	0	0	1	3	3	5			4	10	320	8	0	Grade I	0	0	0	0	4	0	0
5	Asha	24	154	pace	4.5	12	T5	50	T6	91	1:10 PM	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	3	3	5		2	6	375	7	1	Grade I	0	0	0	0	3	0	0
6	Lakshmi	27	160	pace	4	13	T6	45	T6	83	12:11 PM	5	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	1	3	3	3	5		4	10	385	7	1	Grade I	0	0	0	0	2	0	0
7	Amsavall	23	162	pace	4	14	T5	68	T7	65	12:55 PM	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	3	3	5		2	6	350	7	1	Grade I	0	0	0	0	3	0	0
8	Savitha	29	168	pace	4	13	T5	51	T5	102	12:30 PM	4	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	4	5		2	8	368	8	1	Grade I	0	0	0	0	4	0	0
9	Navaneet	29	151	pace	4.5	13	T4	60	T5	91	1:05 PM	5	4	2	1	0	0	0	0	0	0	0	0	0	0	1	2	3	3	4	5		4	10	345	7	1	Grade I	0	0	0	0	3	0	0
10	Selvaga	25	150	pace	4.5	12	T4	45	T5	86	12:33 PM	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	2	3	5		4	8	410	8	1	Grade I	0	0	0	0	3	0	0
11	Latha	23	159	pace	4.5	13	T6	55	T6	60	11:39 PM	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	3	5		4	8	383	7	1	Grade I	0	0	0	0	3	0	0
12	Anjalidev	25	162	pace	4	13	T5	39	T5	87	12:38 PM	5	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	5			3	8	355	8	1	Grade I	0	0	0	0	4	0	0
13	Shalini	26	154	pace	4.5	12	T6	40	T6	82	11:40 PM	5	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	1	3	5			4	10	355	6	0	Grade I	0	0	0	0	3	0	0
14	Priya	22	159	pace	4	13	T6	75	T6	60	11:55 PM	5	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	5		4	8	373	6	1	Grade I	0	0	0	0	3	0	0
15	Jamuna	24	152	pace	4.5	12	T6	81	T7	46	1:30 PM	5	3	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	1	3	5		4	12	370	7	1	Grade I	0	0	0	0	3	0	0
16	Mahalak	28	158	pace	4	12	T5	71	T6	70	12:55 PM	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	3	5		4	8	358	7	1	Grade I	0	0	0	0	3	0	0
17	Anjaman	30	172	pace	4.5	14	T5	88	T7	55	1:12 PM	5	3	2	0	0	0	0	0	0	0	0	0	0	0	0	1	3	3	4	5		4	8	310	6	0	Grade I	0	0	0	0	2	0	0
18	Valli	24	158	pace	4	13	T6	54	T7	62	11:05 AM	5	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	5			3	6	320	6	1	Grade I	0	0	0	0	3	0	0
19	Jennifer	23	160	pace	4	13	T5	31	T5	111	12:47 PM	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	3	5		4	8	360	7	1	Grade I	0	0	0	0	3	0	0
20	Seetha	32	166	pace	4	13	Patient had no sensory blockade even after waiting for 15 , hence converted to spinal anaesthesia - dropped from study																																								